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The Patent Office
Concept House
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Newport
South Wales
NP10 8QQ

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1. Your reference — N.91079

2. Patent application number
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ISIS INNOVATION LIMITED
Ewert House
Ewert Place
Summertown
Oxford
OX2 7SG

Patents ADP number *(if you know it)*

If the applicant is a corporate body, give the country/state of its incorporation — United Kingdom

08618878002

4. Title of the invention — OXIDATION BY HYDROGEN PEROXIDE

5. Name of your agent *(if you have one)*

J. A. KEMP & CO.

"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*

14 South Square
Gray's Inn
London
WC1R 5JJ

Patents ADP number *(if you know it)* — 26001

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Country	Priority application number *(if you know it)*	Date of filing *(day / month / year)*

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Patents Form 1/77

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Continuation sheets of this form	-
Description	75
Claim(s)	2
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Request for a substantive examination (Patents Form 10/77)	-
Any other documents (please specify)	-

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Signature(s) J. A. Kemp & Co J.A. KEMP & CO. Date 23 February 2004

12. Name, daytime telephone number and e-mail address, if any, of person to contact in the United Kingdom

Suleman ALI
020 7405 3292

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OXIDATION BY HYDROGEN PEROXIDE

Field of the Invention

The invention relates to a method of carrying out an oxidation reaction.

Background of the Invention

Monooxygenase enzymes catalyse the oxidation of a very wide range of substrates. In order to catalyse the reaction, a monooxygenase enzyme generally requires a cofactor and at least one electron-transfer partner protein (reductase). However, monooxygenase enzymes are capable of using hydrogen peroxide (H_2O_2) as an oxidizing agent because it acts as a source of dioxygen and two electrons. The use of H_2O_2 to drive oxidation reactions is known as the "peroxide shunt".

Summary of the invention

Monooxygenase enzymes generally have a high K_m for H_2O_2, (such as about 20mM) in comparison to peroxidase enzymes. As a result, high concentrations of H_2O_2 are required for appreciable levels of activity of a monooxygenase enzyme when the oxidation reaction is performed using the peroxide shunt. For example, the initial rate of monooxygenase activity using 50mM H_2O_2 is far below that when the natural co-factor, NAD(P)H, is used as with the physiological electron-transfer partners.

The invention provides a more efficient method of carrying out an oxidation reaction using the peroxide shunt by reducing the oxidative damage that occurs to the monooxygenase enzyme by not allowing excess levels of H_2O_2 to be present whilst the reaction is carried out.

Simultaneous production of H_2O_2 at a rate less than or equal to the rate at which it is used in an oxidation reaction catalysed by monooxygenase results in improved efficiency of the oxidation reaction and an increase in the product yield. Various methods may be used to produce H_2O_2 at the required rate, such as use of an electrochemical reaction, an enzyme or a precursor.

Accordingly, the present invention provides a method of carrying out an oxidation reaction catalysed by a monooxygenase enzyme and using hydrogen peroxide as an oxidant, in which reaction a low level of oxidation damage of the monooxygenase occurs, said method comprising producing the hydrogen peroxide

simultaneously with the oxidation reaction, wherein the hydrogen peroxide is produced at a rate less than or equal to the rate at which it is used in the reaction.

The present invention also provides a method of carrying out an oxidation reaction catalysed by a monooxygenase enzyme and using hydrogen peroxide as an oxidant, in which reaction a low level of oxidation damage of the monooxygenase occurs, said method comprising carrying out the reaction in the presence of an H_2O_2 or hydroxyl radical sequestering agent that controls the H_2O_2 or hydroxyl radical concentration.

Description of the Sequences

SEQ ID NO: 1 shows the nucleotide sequence of cytochrome P450Cam from *Pseudomonas putida.*

SEQ ID NO: 2 shows the amino acid sequence of cytochrome P450Cam from *Pseudomonas putida.*

SEQ ID NO: 3 shows the nucleotide sequence of cytochrome P450BM-3 from *Bacillus megaterium.*

SEQ ID NO: 4 shows the amino acid sequence of cytochrome P450 BM-3 from *Bacillus megaterium*. The first 472 amino acid residues form the heme domain. The last 585 amino acid residues form the reductase domain. All 1048 amino acid residues form the holoenzyme.

The convention in the art, which is adopted herein, is to refer to a mutant with reference to the native amino acid residue at a position in the sequence, followed by the amino acid at that position in the mutant, e. g., F87 refers to the phenylalanine at position 87 in the wild-type sequence, and F87A refers to the phenylalanine at position 87 in the wild-type sequence which has been changed to alanine in the variant. The numbering of the amino acid residues starts with the amino acid residue following the initial methionine residue.

Mutants used in Examples were F87A (single mutation; SEQ ID NOs: 5 and 6) and F87V L188Q A74G (triple mutation; SEQ ID NOs: 7 and 8).

SEQ ID NO: 5 shows the amino acid sequence of the F87A mutant of cytochrome P450BM-3 from *Bacillus megaterium*.

SEQ ID NO: 6 shows the nucleotide sequence of of the F87A mutant of cytochrome P450BM-3 from *Bacillus megaterium*.

SEQ ID NO: 7 shows the amino acid sequence of the F87V L188Q A74G

mutant of cytochrome P450BM-3 from *Bacillus megaterium*.

SEQ ID NO: 8 shows the nucleotide sequence of of the F87V L188Q A74G mutant of cytochrome P450BM-3 from *Bacillus megaterium*.

SEQ ID NO: 9 shows the nucleotide sequence of subunit 1 of B-276 alkene epoxidase from *Nocardia coralline*.

SEQ ID NO: 10 shows the amino acid sequence of subunit 1 of B-276 alkene epoxidase from *Nocardia coralline*.

SEQ ID NO: 11 shows the nucleotide sequence of subunit 2 of B-276 alkene epoxidase from *Nocardia coralline*.

SEQ ID NO: 12 shows the amino acid sequence of subunit 2 of B-276 alkene epoxidase from *Nocardia coralline*.

SEQ ID NO: 13 shows the nucleotide sequence of the alpha subunit of Py2 alkene monooxygenase from *Xanthobacta* sp.

SEQ ID NO: 14 shows the amino acid sequence of the alpha subunit of Py2 alkene monooxygenase from *Xanthobacta* sp.

SEQ ID NO: 15 shows the nucleotide sequence of the beta subunit of Py2 alkene monooxygenase from *Xanthobacta* sp.

SEQ ID NO: 16 shows the amino acid sequence of the beta subunit of Py2 alkene monooxygenase from *Xanthobacta* sp.

SEQ ID NO: 17 shows the nucleotide sequence of the gamma subunit of Py2 alkene monooxygenase from *Xanthobacta* sp.

SEQ ID NO: 18 shows the amino acid sequence of the gamma subunit of Py2 alkene monooxygenase from *Xanthobacta* sp.

SEQ ID NO: 19 shows the nucleotide sequence of the alpha subunit of soluble methane monooxygenase from *Methylococcus capsulatas*.

SEQ ID NO: 20 shows the amino acid sequence of the alpha subunit of soluble methane monooxygenase from *Methylococcus capsulatas*.

SEQ ID NO: 21 shows the nucleotide sequence of the beta subunit of soluble methane monooxygenase from *Methylococcus capsulatas*.

SEQ ID NO: 22 shows the amino acid sequence of the beta subunit of soluble methane monooxygenase from *Methylococcus capsulatas*.

SEQ ID NO: 23 shows the nucleotide sequence of the gamma subunit of soluble methane monooxygenase from *Methylococcus capsulatas*.

SEQ ID NO: 24 shows the amino acid sequence of the gamma subunit of

soluble methane monooxygenase from *Methylococcus capsulatas.*

SEQ ID NO: 25 shows the nucleotide sequence of GPo1 alkane hydroxylase (*Alk*B gene) from *Pseudomonas oleovorans.*

SEQ ID NO: 26 shows the amino acid sequence of GPo1 alkane hydroxylase from *Pseudomonas oleovorans.*

SEQ ID NO: 27 shows the nucleotide sequence of the alpha subunit of toluene 2-monooxygenase from *Burkholderia cepacia.*

SEQ ID NO: 28 shows the amino acid sequence of the alpha subunit of toluene 2-monooxygenase from *Burkholderia cepacia.*

SEQ ID NO: 29 shows the nucleotide sequence of the beta subunit of toluene 2-monooxygenase from *Burkholderia cepacia.*

SEQ ID NO: 30 shows the amino acid sequence of the beta subunit of toluene 2-monooxygenase from *Burkholderia cepacia.*

SEQ ID NO: 31 shows the nucleotide sequence of the gamma subunit of toluene 2-monooxygenase from *Burkholderia cepacia.*

SEQ ID NO: 32 shows the amino acid sequence of the gamma subunit of toluene 2-monooxygenase from *Burkholderia cepacia.*

SEQ ID NO: 33 shows the nucleotide sequence of phenol hydroxylase (pheA) gene from *Bacillus stearothermophilus.*

SEQ ID NO: 34 shows the amino acid sequence of phenol hydroxylase gene from *Bacillus stearothermophilus.*

SEQ ID NO: 35 shows the nucleotide sequence of stearoyl-ACP desaturase from *Helianthus annuus.*

SEQ ID NO: 36 shows the amino acid sequence of stearoyl-ACP desaturase from *Helianthus annuus.*

Detailed description of the Invention

It is to be understood that this invention is not limited to particular embodiments. It is also to be understood that different applications of the disclosed methods may be tailored to the specific needs in the art. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments of the invention only, and is not intended to be limiting.

In addition as used in this specification and the appended claims, the singular forms "a", "an", and "the" include plural referents unless the content clearly

dictates otherwise. Thus, for example, reference to "a substrate" includes two or more substrates, reference to "an enzyme" includes reference to two or more enzymes, and the like.

All publications, patents and patent applications cited herein, whether supra or infra, are hereby incorporated by reference in their entirety.

The methods of the invention enable the oxidation of a variety of substrates. Such substrates include, but are not limited to, alkanes, aromatic compounds, terpenoid compounds, alkenes and fatty acids.

Suitable alkanes include, but are not limited to, methane, ethane, propane, butane, pentane, hexane, heptane, *n*-octane, *n*-nonane, *n*-decane, *n*-dodecane and *n*-hexadecane. The oxidation of alkanes produces alcohols. The oxidation of methane to methanol is technologically and economically very important. The medium-chain alcohols (e.g. *n*-octanol) are synthetic intermediates while the longer chain alcohols (e.g. *n*-dodecanol) are used for the synthesis of fatty acid derivatives.

Suitable aromatic compounds include, but are not limited to, benzene, toluene, xylene, chlorobenzene, phenol and substituents thereof. The phenolic and catecholic products are used in the synthesis of fragrance and flavour compounds.

Suitable terpenoid compounds include, but are not limited to, monoterpenes such as limonene, pinene, terpinene, and ocimene, sesquiterpenes such as valencene and aromadendrene and triterpenes which include the steroidal compounds. The products are intermediates for synthesis, fine fragrance and flavouring chemicals and pharmaceuticals.

Suitable alkenes include, but are not limited to, simple molecules such as propene, hex-1-ene, hex-2-ene, and styrene, and carbon-carbon double bonds in complex molecules. Selective epoxidation of alkenes to a single enantiomer is very important in synthesis. Optically pure propene oxide and styrene oxide are very useful intermediates in synthesis.

Hydroxylated fatty acids are precursors to polymers.

Monooxygenase enzyme

The enzyme used to carry out an oxidation reaction according to the invention is a monooxygenase enzyme. A person skilled in the art can determine whether an enzyme is a monooxygenase enzyme using standard techniques in the art. Typically, the prosthetic groups may be characterised using protein crystallography,

especially for non-heme iron enzymes because they generally do not have chromophores. Otherwise, a person skilled in the art will typically use sequence alignment, looking for conserved motifs such as the active site, and iron content as well as subunit composition.

The monooxygenase enzyme preferably has a K_m for H_2O_2 of at least 15nM, at least 20nM, at least 25nM, at least 30nM, at least 35nM, at least 40nM, at least 45nM or at least 50nM.

Examples of monooxygenase enzymes include, but are not limited to, cytochrome P450 monooxygenases and non-heme di-iron monooxygenase enzymes. Suitable non-heme di-iron monooxygenase enzymes include, but are not limited to methane monooxygenase (Colby *et al.*, Biochem. J., 1977; 165: 395-402; Dalton, Adv. Appl. Microbiol., 1980; 26: 71-87; Fox *et al.*, J. Biol. Chem., 1989; 264: 10023-10033; Fox *et al.*, Methods Enzymol., 1990; 188: 191-202; McDonald *et al.*, Appl. Environ. Microbiol., 1997; 63: 1898-1904), alkane hydroxylase (van Beilen *et al.*, Enzyme Microb. Technol., 1994; 16: 904-911), toluene monooxygenase (Luykx *et al.*, Biochem. Biophys. Res. Commun., 2003; 312: 373-379; Pikus *et al.*, Biochemistry, 1996; 35: 9106-9119; Newman & Wackett, Biochemistry, 1995; 34: 14066-14076), alkene monooxygenase (Gallagher *et al.*, Eur. J. Biochem., 1997; 247: 635-641; Lange & Que, Curr. Opin. Chem. Biol., 1998; 2: 159-172; Zhou *et al.*, FEBS Lett., 1998; 430: 181-185), phenol monooxygenase (Divari *et al.*, Eur. J. Biochem., 2003; 270: 2244-2253) and steroid desaturase (Shanklin *et al.*, Biochemistry, 1994; 33: 12787-12794). The non-heme di-iron monooxygenase enzymes are typically of eukaryotic or prokaryotic origin and preferably of bacterial, fungal, yeast, plant or animal origin. Preferred sequences are shown in SEQ ID NOs: 1 to 36.

The enzyme used in the methods of the invention is preferably a cytochrome P450 enzyme, typically of eukaryotic or prokaryotic origin. Cytochrome P450 monooxygenases are typically characterised by a 446-450 nm heme Soret band for the ferrous-carbon monoxide complex. The enzyme is generally of bacterial, fungal, yeast, plant or animal origin, and thus may be from a bacterium of the genus *Pseudomonas*. The enzyme may be a naturally-occurring form of P450, such as $P450_{cam}$, $P450_{BM-3}$ from *Bacillus megaterium*, $P450_{terp}$ from *Pseudomonas sp*, $P450_{eryF}$ from *Saccharopollyspora erythraea* and also P450 105 D1 (CYP105) from *Streptomyces griseus* strains.

Alternatively, the enzyme may be a mutant of a naturally-occurring form of P450. The mutants retain the essential biological activity of the naturally-occurring enzyme, namely the ability to catalyse an oxidation reaction using H_2O_2. The mutant may have one or more mutations in the active site of the enzyme.

An amino acid 'in the active site' is one which lines or defines the site in which the substrate is bound during catalysis or one which lines or defines a site through which the substrate must pass before reaching the catalytic site. Therefore such an amino acid typically interacts with the substrate during entry to the catalytic site or during catalysis. Such an interaction typically occurs through an electrostatic interaction (between charged or polar groups), hydrophobic interaction, hydrogen bonding or van der Waals forces.

The amino acids in the active site can be identified by routine methods to those skilled in the art. These methods include labelling studies in which the enzyme is allowed to bind a substrate which modifies ('labels') amino acids which contact the substrate. Alternatively the crystal structure of the enzyme with bound substrate can be obtained in order to deduce the amino acids in the active site.

The monooxygenase enzyme may have 1, 2, 3, 4, 5 to 10, 10 to 20 or more other mutations, such as substitutions, insertions or deletions. Amino acid substitutions may be made to the amino acid sequence of a naturally-occurring enzyme, for example from 1, 2, 3, 4 or 5 to 10, 20 or 30 substitutions. Conservative substitutions may be made, for example, according to Table 1. Amino acids in the same block in the second column and preferably in the same line in the third column may be substituted for each other:

Table 1 – Conservative amino acid substitutions

NON-AROMATIC	Non-polar	G A P
		I L V
	Polar – uncharged	C S T M
		N Q
	Polar - charged	D E
		H K R
AROMATIC		H F W Y

The mutations may be in the active site or outside the active site. Typically the mutations are in the 'second sphere' residues which affect or contact the position or orientation of one or more of the amino acids in the active site. The insertion is typically at the N and/or C terminal and thus the enzyme may be part of a chimeric protein. The deletion typically comprises the deletion of amino acids which are not involved in catalysis, such as those outside the active site (thus the enzyme is a mutated fragment of a naturally occurring enzyme). The monooxygenase enzyme may thus comprise only those amino acids which are required for oxidation activity.

The mutation in the active site typically alters the position and/or conformation of the substrate when it is bound in the active site. The mutation may make the site on the substrate which is to be oxidized more accessible to the heme group. Thus the mutation may be a substitution to an amino acid which has a smaller or larger, or more or less polar, side chain.

The mutations typically increase the stability of the protein, or make it easier to purify the protein. They typically prevent the dimerisation of the protein, typically by removing cysteine residues from the protein (e.g. by substitution of cysteine at position 334 of $P450_{cam}$, or at an equivalent position in a homologue, preferably to alanine). They typically allow the protein to be prepared in soluble form, for example by the introduction of deletions or a poly-histidine tag, or by mutation of the N-terminal membrane anchoring sequence. The mutations typically inhibit protein oligomerisation, such as oligomerisation arising from contacts between hydrophobic patches on protein surfaces.

The mutations may affect the manner in which the enzyme utilises H_2O_2 and thereby improve the efficiency of the reaction. For example, mutants of the P450 enzyme from *Pseudomonas putida* hydroxylate napthalene through the "peroxide shunt" with more than a 20-fold increase in the activity of the enzyme (Joo *et al.*, Nature, 1999; 399(6737): 636-637). In addition, replacement of all the methionine residues of the heme domain of $P450_{BM-3}$ with norleucine results in a two-fold increase in the peroxygenase activity of the enzyme (Cirino *et al.*, Biotechnol. Bioeng., 2003; 83(6): 729-734). Furthermore, direct evolution studies to find mutants of enzymes more resistant to peroxide (Cirino & Arnold, Angew. Chem. Int. Ed., 2003; 42: 3299-3301).

Thus the mutant enzyme is typically at least 70% homologous to a naturally occurring enzyme on the basis of amino acid identity.

A mutant protein (i.e. described as being a mutant of another protein) mentioned herein is typically at least 70% homologous to the relevant protein or at least 80 or 90% and more preferably at least 95%, 97% or 99% homologous thereto over at least 20, preferably at least 30, for instance at least 40, 60 or 100 or more contiguous amino acids. The contiguous amino acids may include the active site. This homology may alternatively be measured not over contiguous amino acids but over only the amino acids in the active site.

Homology can be measured using known methods. For example the UWGCG Package provides the BESTFIT program which can be used to calculate homology (for example used on its default settings) (Devereux *et al* (1984) *Nucleic Acids Research* **12**, p387-395). The PILEUP and BLAST algorithms can be used to calculate homology or line up sequences (typically on their default settings), for example as described in Altschul S. F. (1993) J Mol Evol 36:290-300; Altschul, S, F *et al* (1990) J Mol Biol 215:403-10.

Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information (http://www.ncbi.nlm.nih.gov/). This algorithm involves first identifying high scoring sequence pair (HSPs) by identifying short words of length W in the query sequence that either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighbourhood word score threshold (Altschul *et al*, supra). These initial neighbourhood word hits act as seeds for initiating searches to find HSPs containing them. The word hits are extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Extensions for the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment. The BLAST program uses as defaults a word length (W) of 11, the BLOSUM62 scoring matrix (see Henikoff and Henikoff (1992) *Proc. Natl. Acad. Sci.* USA 89: 10915-10919) alignments (B) of 50, expectation (E) of 10, M=5, N=4, and a comparison of both strands.

The BLAST algorithm performs a statistical analysis of the similarity between two sequences; see e.g., Karlin and Altschul (1993) *Proc. Natl. Acad. Sci.*

USA 90: 5873-5787. One measure of similarity provided by the BLAST algorithm is the smallest sum probability (P(N)), which provides an indication of the probability by which a match between two nucleotide or amino acid sequences would occur by chance. For example, a sequence is considered similar to another sequence if the smallest sum probability in comparison of the first sequence to the second sequence is less than about 1, preferably less than about 0.1, more preferably less than about 0.01, and most preferably less than about 0.001.

Mutants include fragments of the above-mentioned sequences. Such fragments retain monooxygenase activity. Fragments may be at least 300, at least 400 or at least 450 amino acids in length. Such fragments may be used to produce chimeric enzymes as described in more detail below.

Mutants also include chimeric proteins comprising fragments or portions of a naturally-occurring enzyme. One or more amino acids may be alternatively or additionally added to the polypeptides described above. An extension may be provided at the N-terminus or C-terminus of the naturally-occurring enzyme or variant or fragment thereof. The extension may be quite short, for example from 1 to 10 amino acids in length. Alternatively, the extension may be longer. A carrier protein may be fused to an amino acid sequence described above. A fusion protein incorporating one of the enzymes described above can thus be used in the invention.

The naturally-occurring enzyme or mutant thereof may also be chemically-modified. A number of side chain modifications are known in the art and may be made to the side chains of the enzymes discussed above. Such modifications include, for example, glycosylation, phosphorylation, modifications of amino acids by reductive alkylation by reaction with an aldehyde followed by reduction with $NaBH_4$, amidination with methylacetimidate or acylation with acetic anhydride. The modification is preferably glycosylation.

The mutations discussed herein are generally introduced into the enzyme by using methods known in the art, such as site directed mutagenesis of the enzyme, PCR and gene shuffling methods or by the use of multiple mutagenic oligonucleotides in cycles of site-directed mutagenesis. Thus the mutations may be introduced in a directed or random manner. The mutagenesis method thus produces one or more polynucleotides encoding one or more different mutants. Typically a library of mutant oligonucleotides is produced which can be used to produce a library of mutant enzymes.

The enzyme may be made synthetically or by recombinant means using methods known in the art. The amino acid sequence of the monooxygenase enzyme may be modified to include non-naturally occurring amino acids or to increase the stability of the enzyme. When the enzyme is produced by synthetic means, such amino acids may be introduced during production. The proteins or peptides may also be modified following either synthetic or recombinant production.

The enzyme may also be produced using D-amino acids. In such cases the amino acids will be linked in reverse sequence in the C to N orientation. This is conventional in the art for producing such proteins or peptides.

The enzyme may be produced in a cell by *in situ* expression of the polypeptide from a recombinant expression vector. The expression vector optionally carries an inducible promoter to control the expression of the polypeptide. The enzyme may be produced in large scale following purification by any protein liquid chromatography system after recombinant expression. Preferred protein liquid chromatography systems include FPLC, AKTA systems, the Bio-Cad system, the Bio-Rad BioLogic system and the Gilson HPLC system.

Oxidation reaction

The methods of the invention concerns carrying out a high efficiency oxidation reaction catalysed by a monooxygenase enzyme. A high efficiency oxidation reaction is a reaction that occurs without an appreciable reduction in the enzyme turnover or product yield or inactivation of the monooxygenase enzyme. Preferably, the monooxygenase enzyme displays at least 70%, at least 80%, at least 90%, at least 95% or 100% of the activity shown at the beginning of the reaction after 1 hour, 2 hours, 6 hours, 12 hours, 1 day, 2 days or 5 days.

Typically the methods of the invention are carried out in vitro, such as in a cell free system.

The reaction is driven by the "peroxide shunt". The reaction of the invention is carried out in the presence of the monooxygenase enzyme (a), the substrate (b) and H_2O_2 (c). The reaction is typically performed in aerobic conditions and does not require any cofactors. The production of (c) is discussed in more detail below. In this system the flow of electrons is typically: (c) → (a) → (b).

In the methods the concentration of (a) and (b) is typically from 10^{-8} to 10^{-2}M, preferably from 10^{-6} to 10^{-4}M. Typically the ratio of concentrations of (a): (b) is

from 0.1:10 to 1:10, preferably from 1:0.5 to 1:2, or from 1:0.8 to 1:1.2. Preferably, the concentration of (b) is greater than the concentration of (a). The preferred concentration of (a) is that which when reacted with substrate will generate sufficient product to be detected by available analytical methods e.g. GC, HPLC. This is typically of the order of μM quantities.

Generally the methods are carried out at a temperature and/or pH at which the monooxygenase enzyme is functional, such as when the enzyme has at least 20%, 50%, 80% or more of peak activity. Typically the pH is from 2 to 11, such as from 5 to 9 or from 6 to 8, preferably from 7 to 7.8 or 7.4. The pH can be maintained using a suitable buffering agent such as phosphate or acetate based systems. Typically the temperature is from 0 to 80°C, such as from 25 to 75°C, from 30 to 60°C or from 50°C to 80°C. Preferably, the temperature is from 20 to 40°C.

Typically in the methods at least 20 turnovers/min occur, such as at least 50, 100, 200, 300, 500 or more turnovers (turnover is measured as nanomoles of product formed per nanomole of enzyme).

Typically, the rate of H_2O_2 production is less than or equal to 1, 2 or 3 μg per min per mg of monooxygenase enzyme. Typically, the concentration of H_2O_2 throughout the reaction is less than or equal to 0.1, 0.5 or 1mM. Typically, the reaction continues for at least 60 minutes, at least 240 minutes, at least 6 hours or at least 10 hours.

The methods of the invention may be carried out in the monooxygenase substrate if it is a liquid under the reaction conditions. The methods of the invention may also be conducted in a solvent. Suitable solvents include, but are not limited to, water, aqueous buffer solutions mixed water/organic and aqueous buffer/organic solvent systems. Preferably, the organic solvent is a hydrocarbon such as hexane, benzene, acetonitrile, lower aliphatic alcohols, ketones and dioxane, dimethylformamide and dimethylsulphoxide and mixtures thereof. The solvent is typically one in which the reagants and products are highly soluble and one that maintains the stability and activity of the monooxygenase enzyme.

The reaction may be carried out in a homogenous system with all the components in solution. Typically, the monooxygenase enzyme and substrate are mixed together in a suitable solvent in a stirred tank reactor and the reaction is conducted in batch, semi-batch or continuous mode.

Alternatively, the monooxygenase enzyme may be immobilized on a suitable solid support, such as silica, prior to carrying out the method of the invention. An immobilized monooxygenase enzyme can be packed into a fixed bed reactor and the substrate passed over the enzyme. In one embodiment, the enzyme producing the H_2O_2 (discussed in more detail below) may be immobilized on the same or different material as the monooxygenase enzyme. Procedures for immobilizing enzymes are known in the art. Examples of such procedures include, but are not limited to, covalent coupling to insoluble organic or inorganic supports, entrapment in gels and adsorption to ion exchange resins or other adsorbent materials. (G. F. Bickerstaff ed., "Immobilization of Enzymes and Cells," Humana Press, Totowa. New Jersey, 1997).

In a further embodiment, a membrane on the "entry" side admits the substrate slowly from the "reactant" side and then a hydrophilic membrane on the "exit" side allows hydrophilic compounds to flow out to the "product" side of the flow reaction cell. In this case the H_2O_2 may be generated outside the membrane and allowed to flow through the membrane to the mobile or immobile enzyme.

In one embodiment, H_2O_2 is preferably produced by one of the methods discussed in more detail below. In another embodiment, a H_2O_2 or hydroxyl radical sequestering agent is used to sequester excess H_2O_2 or hydroxyl radical during the oxidation reaction. The sequestering agent may be a chelating agent. In one embodiment, the chelating agent is EDTA. The EDTA inhibits production of the hydroxyl radical, for example, produced by the reaction of trace amounts of iron (or copper) with the H_2O_2.

H_2O_2 production by an electrochemical reaction

The H_2O_2 may be produced in the method of the invention by an electrochemical reaction. An electrochemical reaction is generally a means for introducing a current to a liquid, preferably a solution. An electrochemical reaction is typically an oxidation or reduction reaction that takes place at an electrode through which a current flows. An electrode is a solid capable of conducting electricity, typically carbon-based or metallic, leading to an external source or sink which is in contact with the liquid, preferably a solution. The electrode may be either positively charged (cathode) or negatively charged (anode). Two or more electrodes may form an electrochemical cell from which an external wire can lead from each electrode to

an external electrical device. An oxidation or reduction reaction takes place at one electrode, while a redox reaction can take place either in an electrochemical cell or directly in the liquid.

Production of H_2O_2 using an electrochemical reaction is energy efficient. H_2O_2 is typically produced by the controlled electrochemical reduction of molecular oxygen to hydrogen peroxide. The surface area and the overpotential of the cathode are key considerations for the two-electron reduction of molecular oxygen to hydrogen peroxide. Typically, carbon-based cathodes are used and they may be modified with a compound known to lower the overpotential for this reaction. Electrode materials and modifiers which will perform this task effectively and efficiently are well known in the art. The reduction of O_2, and hence production of hydrogen peroxide, can typically be controlled by the potential applied to the cathode. The potential applied to the cathode will vary depending on the cathode and any modifications to the cathode made.

The electrochemical reaction used in the method of the invention may be the sonoelectrochemical reduction of dioxygen. This method is well known in the art (Compton *et al.*, Electroanalysis, 1997; 9(7): 509-522).

H_2O_2 production by an enzyme

The H_2O_2 may be produced in the method of the invention by an enzyme. The enzyme is preferably an oxidase. Examples of suitable oxidases include, but are not limited to, glucose oxidase (E.C. 1.1.3.4), secondary-alcohol oxidase (E.C. 1.1.3.18), methanol oxidase (E.C. 1.1.3.31), oxalate oxidase (E.C. 1.2.3.4), aryl-aldehyde oxidase (E.C. 1.2.3.9), carbon monoxide oxidase (E.C. 1.2.3.10), amine oxidase (E.C. 1.4.3.4), ethanolamine oxidase (E.C. 1.4.3.8), nitroethane oxidase (E.C. 1.7.3.1) and sulfite oxidase (E.C. 1.8.3.1). Glucose oxidase (E.C. 1.1.3.4) catalyzes the conversion of D-glucose to D-glucono-1,5-lactone and H_2O_2. Secondary-alcohol oxidase (E.C. 1.1.3.18) catalyzes the conversion of a secondary alcohol to a ketone and H_2O_2. Methanol oxidase (E.C. 1.1.3.31) catalyzes the conversion of methanol to formaldehyde and H_2O_2. Oxalate oxidase (E.C. 1.2.3.4) catalyzes the conversion of oxalate to carbon dioxide and H_2O_2. Aryl-aldehyde oxidase (E.C. 1.2.3.9) catalyzes the conversion of an aromatic aldehyde to an aromatic acid and H_2O_2. Carbon monoxide oxidase (E.C. 1.2.3.10) catalyzes the conversion of CO and H_2O to carbon dioxide and H_2O_2. Amine oxidase (E.C.

1.4.3.4) catalyzes the conversion of RCH_2NH_2 and H_2O to RCHO and NH_3 and H_2O_2. Ethanolamine oxidase (E.C. 1.4.3.8) catalyzes the conversion of ethanolamine and H_2O to glycolaldehyde and H_2O_2. Nitroethane oxidase (E.C. 1.7.3.1) catalyzes the conversion of nitroethane and H_2O to acetaldehyde and H_2O_2. Sulfite oxidase (E.C. 1.8.3.1) catalyzes the conversion of sulfite and H_2O_2 to sulfate and H_2O_2. The oxidase may be purchased commercially (e.g., glucose oxidase). Alterantively, the oxidase can be extracted from known microorganisms using procedures known in the art.

The substrate for the oxidase will be well known in the art. In addition to the substrate, the reaction to produce H_2O_2 will also involve water. Typically, a H_2O_2-activating metal is also included in the reaction. Suitable metals include, but are not limited to, cerium, chromium, cobalt, copper, iron, manganese, molybdenum, silver, titanium, tungsten, vanadium and mixtures thereof. Metallosilicates containing the above metals can be prepared and used in the method of the invention. The procedure for producing such metallosilicates in known in the art (Neumann *et al.*, Journal of Catalysis, 1997; 166: 206-127). The metallosilicate is preferably tetrahedrally coordinated titanium such as silicalite-l (TS-1), silicalite-2 (TS-2), zeolite-beta, silicon analogs of ZSM-48 and MCM-4 1. (Murugavel and Roesky, Angew. Chem. Int. Ed. Engl., 1997; 36(5): 477-479).

In a preferred embodiment of the invention, the metal-containing solid or metallosilicate is used as a support upon which the H_2O_2-producing enzyme is immobilized. In another preferred embodiment, the monooxygenase enzyme is also immobilized on the same or different metallosilicate.support.

Preferably, the oxidase is first mixed with the other reaction components and then the reaction is initiated by addition of the oxidase substrate. For example, the monooxygenase enzyme, monoxygenase enzyme substrate and oxidase are all mixed and then the oxidase enzyme is added. In a preferred embodiment, $P450_{BM3}$, octane and glucose oxidase are mixed together and then glucose added. Control of H_2O_2 generation can typically be accomplished by controlling the rate at which the oxidase substrate is added.

H_2O_2 production by a precursor

The H_2O_2 may be produced in the method of the invention by a precursor. The generation of H_2O_2 by the addition of a precursor to water is well known in the

art. Precursors include, but are not limited to, salts of perborate, salts of percarbonate, salts of perphosphate and peroxynitrite. Preferred precursors are sodium salts. The H_2O_2-producing properties of the precursor may be enhanced by using a compound such as tetraacetylethylenediamine. The amount of precursor added to the solution containing the monoxygenase enzyme and substrate is such to maximise the enzymatic reaction with the substrate and to minimise the deactivation of the enzyme by H_2O_2. Preferably the concentration of H_2O_2 produced does not exceed the K_m value for the enzyme but is sufficient to generate the enzyme reactive species.

Examples

Example 1

In this experiment, octane was reacted with electrochemically generated H_2O_2 in the presence of $P450_{BM3}$ heme domain. The experiment was performed at room temperature with a three-electrode configuration in a 100 mL glass beaker. The reticulated vitreous carbon (RVC) cathode, platinum gauze anode and Ag/AgCl reference electrode were contained in the one vessel. The RVC cathode was briefly immersed in a 1 mM 2-aminoanthraquinone ethanolic solution before being removed and allowed to dry in air. The reaction solution contained aqueous Tris buffer (50 mM, pH 7.4) saturated with oxygen, 0.2 M KCl, 0.5 mM octane, and 3 μM $P450_{BM3}$ F87V L188Q A74G heme domain. The reaction solution was stirred to equilibrate (5-10 minutes) and then a potential of –0.55 V vs Ag/AgCl was applied for 2 hours and the solution stirred continuously throughout. GC analysis revealed the presence of the solvent chloroform, octane, 2-, 3- and 4-octanol and the internal standard 1-nonanol. The relative proportion of 2, 3 & 4-octanol was 1:1.1:0.7. The total concentration of octanols formed was 141 μM, representing a turnover per enzyme of 47.

A similar experiment was performed with 1.43 μM wild-type $P450_{BM3}$ heme domain. The total concentration of octanols formed was 8.4 μM, representing a turnover per enzyme of 6. The relative proportion of 2, 3 & 4-octanol in this case was 1:1.7:2.0.

Example 2

In this experiment, octane was reacted with enzymatically generated H_2O_2 in the presence of $P450_{BM3}$ holoenzyme. Into a glass vial was added a solution (total volume 5 mL) consisting of aqueous Tris buffer (50 mM, pH 7.4), 0.5 mM octane, 1.6 μM $P450_{BM3}$ F87V L188Q A74G holoenzyme and glucose oxidase (1.5 U). After equilibration (5 mins), the reaction was initiated by addition of glucose (1×10^{-6} moles). Successive additions of glucose (1×10^{-6} moles) were made every 5 minutes up to 1 hour (total of 12 additions equivalent to 1.2×10^{-5} moles). The reaction was stirred continuously during this time and stopped after 1.5 hours. GC analysis revealed the presence of the solvent chloroform, octane, 2-, 3- and 4-octanol and the internal standard 1-nonanol. The relative proportion of 2, 3 & 4-octanol was 1:1.1:0.8. The total concentration of octanols formed was 17 μM, representing a turnover per enzyme of 10.

Example 3

In this experiment, octane was reacted with H_2O_2 derived from sodium perborate, in the presence of $P450_{BM3}$ holoenzyme. Into a glass vial was added a solution (total volume 5 mL) consisting of aqueous Tris buffer (40 mM, pH 7.4), 0.5 mM octane, and 1.3 μM $P450_{BM3}$ F87V L188Q A74G holoenzyme. After equilibration (5 mins), the reaction was initiated by addition of $NaBO_3.4H_2O$ (1×10^{-4} moles) and stirred continuously for 1 hour. GC analysis revealed the presence of the solvent chloroform, octane, 2-, 3- and 4-octanol and the internal standard 1-nonanol. The relative proportion of 2, 3 & 4-octanol was 1:1.8:1.1. The total concentration of octanols formed was 77 μM, representing a turnover per enzyme of 59.

For Examples 1 to 3, no octanol products were observed when the P450 enzyme was absent from the solution.

Example 4

In this experiment, pinene was reacted with H_2O_2 derived from sodium perborate, in the presence of $P450_{BM3}$ heme domain. Into a glass vial was added a solution (total volume 5 mL) consisting of aqueous Tris buffer (40 mM, pH 7.4), 0.63 mM pinene, and 3.7 μM wild-type $P450_{BM3}$ heme domain. After equilibration (5 mins), the reaction was initiated by addition of 7.8×10^{-6} moles $NaBO_3.4H_2O$ and

stirred continuously for 1 hour. GC analysis revealed the presence of *cis/trans* 2,3-epoxides (32%), (+)-*trans*-verbenol (16%), (+)-*cis*-verbenol (6%), (+)-verbenone/(+)-myrtenol (13%), myrtenal (4%), as well as unidentified further oxidation products (29%). The total concentration of products formed was 80 μM, representing a turnover per enzyme of 22.

Example 5

In this experiment, phenol monooxygenase is reacted with phenol in the presence of with H_2O_2 generated by sodium perborate. Into a glass vial is added a solution (total volume 5 mL) consisting of aqueous Tris buffer (40 mM, pH 7.4), 0.63 mM phenol, and 3.7 μM wild-type phenol monooxygenase. After equilibration (5 mins), the reaction is initiated by addition of 7.8×10^{-6} moles $NaBO_3.4H_2O$ and stirred continuously for 1 hour. GC analysis reveals the presence of oxidation products.

Example 6

In this experiment, $P450_{BM3}$ is reacted with palmitic acid in the presence of H_2O_2 generated by glucose oxidase. Into a glass vial is added a solution (total volume 5 mL) consisting of aqueous Tris buffer (50 mM, pH 7.4), 0.5 mM palmitic acid, 1.6 μM $P450_{BM3}$ holoenzyme and glucose oxidase (1.5 U). After equilibration (5 mins), the reaction is initiated by addition of glucose (1×10^{-6} moles). Successive additions of glucose (1×10^{-6} moles) are made every 5 minutes up to 1 hour (total of 12 additions equivalent to 1.2×10^{-5} moles). The reaction is stirred continuously during this time and stopped after 1.5 hours. GC analysis reveals the presence of oxidation products.

Example 7

Plant CYP74C is reacted with 13 S-hydroperoxylinolenic acid to form the compound 3Z-hexenal (a fragrance). The H_2O_2 is generated by sodium perborate. Into a glass vial is added a solution (total volume 5 mL) consisting of aqueous Tris buffer (40 mM, pH 7.4), 0.63 mM 13 S-hydroperoxylinolenic acid, and 3.7 μM wild-type plant CYP74C. After equilibration (5 mins), the reaction is initiated by addition of 7.8×10^{-6} moles $NaBO_3.4H_2O$ and stirred continuously for 1 hour. GC analysis

reveals the presence of oxidation products.

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acg ctt gat aca att ggt ctt tgc ggc ttt aac tat cgc ttt aac agc      2035
Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr Arg Phe Asn Ser
150                 155                 160                 165

ttt tac cga gat cag cct cat cca ttt att aca agt atg gtc cgt gca      2083
Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Thr Ser Met Val Arg Ala
                170                 175                 180

ctg gat gaa gca atg aac aag ctg cag cga gca aat cca gac gac cca      2131
Leu Asp Glu Ala Met Asn Lys Leu Gln Arg Ala Asn Pro Asp Asp Pro
            185                 190                 195

gct tat gat gaa aac aag cgc cag ttt caa gaa gat atc aag gtg atg      2179
Ala Tyr Asp Glu Asn Lys Arg Gln Phe Gln Glu Asp Ile Lys Val Met
        200                 205                 210

aac gac cta gta gat aaa att att gca gat cgc aaa gca agc ggt gaa      2227
Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys Ala Ser Gly Glu
    215                 220                 225

caa agc gat gat tta tta acg cat atg cta aac gga aaa gat cca gaa      2275
Gln Ser Asp Asp Leu Leu Thr His Met Leu Asn Gly Lys Asp Pro Glu
230                 235                 240                 245

acg ggt gag ccg ctt gat gac gag aac att cgc tat caa att att aca      2323
Thr Gly Glu Pro Leu Asp Asp Glu Asn Ile Arg Tyr Gln Ile Ile Thr
                250                 255                 260

ttc tta att gcg gga cac gaa aca aca agt ggt ctt tta tca ttt gcg      2371
Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu Leu Ser Phe Ala
            265                 270                 275

ctg tat ttc tta gtg aaa aat cca cat gta tta caa aaa gca gca gaa      2419
Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln Lys Ala Ala Glu
        280                 285                 290

gaa gca gca cga gtt cta gta gat cct gtt cca agc tac aaa caa gtc      2467
Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser Tyr Lys Gln Val
    295                 300                 305

aaa cag ctt aaa tat gtc ggc atg gtc tta aac gaa gcg ctg cgc tta      2515
Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu Ala Leu Arg Leu
310                 315                 320                 325

tgg cca act gct cct gcg ttt tcc cta tat gca aaa gaa gat acg gtg      2563
Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala Lys Glu Asp Thr Val
                330                 335                 340

ctt gga gga gaa tat cct tta gaa aaa ggc gac gaa cta atg gtt ctg      2611
Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu Leu Met Val Leu
            345                 350                 355

att cct cag ctt cac cgt gat aaa aca att tgg gga gac gat gtg gaa      2659
Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly Asp Asp Val Glu
        360                 365                 370

gag ttc cgt cca gag cgt ttt gaa aat cca agt gcg att ccg cag cat      2707
Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala Ile Pro Gln His
    375                 380                 385

gcg ttt aaa ccg ttt gga aac ggt cag cgt gcg tgt atc ggt cag cag      2755
Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys Ile Gly Gln Gln
390                 395                 400                 405

ttc gct ctt cat gaa gca acg ctg gta ctt ggt atg atg cta aaa cac      2803
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Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met Met Leu Lys His
                410                 415                 420

ttt gac ttt gaa gat cat aca aac tac gag ctg gat att aaa gaa act      2851
Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp Ile Lys Glu Thr
            425                 430                 435

tta acg tta aaa cct gaa ggc ttt gtg gta aaa gca aaa tcg aaa aaa      2899
Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala Lys Ser Lys Lys
        440                 445                 450

att ccg ctt ggc ggt att cct tca cct agc act gaa cag tct gct aaa      2947
Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu Gln Ser Ala Lys
    455                 460                 465

aaa gta cgc aaa aag gca gaa aac gct cat aat acg ccg ctg ctt gtg      2995
Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr Pro Leu Leu Val
470                 475                 480                 485

cta tac ggt tca aat atg gga aca gct gaa gga acg gcg cgt gat tta      3043
Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr Ala Arg Asp Leu
                490                 495                 500

gca gat att gca atg agc aaa gga ttt gca ccg cag gtc gca acg ctt      3091
Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln Val Ala Thr Leu
            505                 510                 515

gat tca cac gcc gga aat ctt ccg cgc gaa gga gct gta tta att gta      3139
Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala Val Leu Ile Val
        520                 525                 530

acg gcg tct tat aac ggt cat ccg cct gat aac gca aag caa ttt gtc      3187
Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala Lys Gln Phe Val
    535                 540                 545

gac tgg tta gac caa gcg tct gct gat gaa gta aaa ggc gtt cgc tac      3235
Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys Gly Val Arg Tyr
550                 555                 560                 565

tcc gta ttt gga tgc ggc gat aaa aac tgg gct act acg tat caa aaa      3283
Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr Thr Tyr Gln Lys
                570                 575                 580

gtg cct gct ttt atc gat gaa acg ctt gcc gct aaa ggg gca gaa aac      3331
Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys Gly Ala Glu Asn
            585                 590                 595

atc gct gac cgc ggt gaa gca gat gca agc gac gac ttt gaa ggc aca      3379
Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp Phe Glu Gly Thr
        600                 605                 610

tat gaa gaa tgg cgt gaa cat atg tgg agt gac gta gca gcc tac ttt      3427
Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val Ala Ala Tyr Phe
    615                 620                 625

aac ctc gac att gaa aac agt gaa gat aat aaa tct act ctt tca ctt      3475
Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser Thr Leu Ser Leu
630                 635                 640                 645

caa ttt gtc gac agc gcc gcg gat atg ccg ctt gcg aaa atg cac ggt      3523
Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala Lys Met His Gly
                650                 655                 660

gcg ttt tca acg aac gtc gta gca agc aaa gaa ctt caa cag cca ggc      3571
Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu Gln Gln Pro Gly
            665                 670                 675

agt gca cga agc acg cga cat ctt gaa att gaa ctt cca aaa gaa gct      3619
Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu Pro Lys Glu Ala
        680                 685                 690

tct tat caa gaa gga gat cat tta ggt gtt att cct cgc aac tat gaa      3667
Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro Arg Asn Tyr Glu
    695                 700                 705

gga ata gta aac cgt gta aca gca agg ttc ggc cta gat gca tca cag      3715
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Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu Asp Ala Ser Gln
710                 715                 720                 725

caa atc cgt ctg gaa gca gaa gaa gaa aaa tta gct cat ttg cca ctc    3763
Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala His Leu Pro Leu
                730                 735                 740

gct aaa aca gta tcc gta gaa gag ctt ctg caa tac gtg gag ctt caa    3811
Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr Val Glu Leu Gln
            745                 750                 755

gat cct gtt acg cgc acg cag ctt cgc gca atg gct gct aaa acg gtc    3859
Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala Ala Lys Thr Val
        760                 765                 770

tgc ccg ccg cat aaa gta gag ctt gaa gcc ttg ctt gaa aag caa gcc    3907
Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu Glu Lys Gln Ala
    775                 780                 785

tac aaa gaa caa gtg ctg gca aaa cgt tta aca atg ctt gaa ctg ctt    3955
Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met Leu Glu Leu Leu
790                 795                 800                 805

gaa aaa tac ccg gcg tgt gaa atg aaa ttc agc gaa ttt atc gcc ctt    4003
Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu Phe Ile Ala Leu
                810                 815                 820

ctg cca agc ata cgc ccg cgc tat tac tcg att tct tca tca cct cgt    4051
Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser Ser Ser Pro Arg
            825                 830                 835

gtc gat gaa aaa caa gca agc atc acg gtc agc gtt gtc tca gga gaa    4099
Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val Val Ser Gly Glu
        840                 845                 850

gcg tgg agc gga tat gga gaa tat aaa gga att gcg tcg aac tat ctt    4147
Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala Ser Asn Tyr Leu
    855                 860                 865

gcc gag ctg caa gaa gga gat acg att acg tgc ttt att tcc aca ccg    4195
Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe Ile Ser Thr Pro
870                 875                 880                 885

cag tca gaa ttt acg ctg cca aaa gac cct gaa acg ccg ctt atc atg    4243
Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr Pro Leu Ile Met
                890                 895                 900

gtc gga ccg gga aca ggc gtc gcg ccg ttt aga ggc ttt gtg cag gcg    4291
Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly Phe Val Gln Ala
            905                 910                 915

cgc aaa cag cta aaa gaa caa gga cag tca ctt gga gaa gca cat tta    4339
Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly Glu Ala His Leu
        920                 925                 930

tac ttc ggc tgc cgt tca cct cat gaa gac tat ctg tat caa gaa gag    4387
Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu Tyr Gln Glu Glu
    935                 940                 945

ctt gaa aac gcc caa agc gaa ggc atc att acg ctt cat acc gct ttt    4435
Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu His Thr Ala Phe
950                 955                 960                 965

tct cgc atg cca aat cag ccg aaa aca tac gtt cag cac gta atg gaa    4483
Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln His Val Met Glu
                970                 975                 980

caa gac ggc aag aaa ttg att gaa ctt ctt gat caa gga gcg cac ttc    4531
Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln Gly Ala His Phe
            985                 990                 995

tat att tgc  gga gac gga agc caa  atg gca cct gcc gtt  gaa gca    4576
Tyr Ile Cys  Gly Asp Gly Ser Gln  Met Ala Pro Ala Val  Glu Ala
        1000                1005                1010

acg ctt atg  aaa agc tat gct gac  gtt cac caa gtg agt  gaa gca    4621
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Thr Leu Met  Lys Ser Tyr Ala Asp  Val His Gln Val Ser  Glu Ala
        1015                1020                1025

gac gct cgc  tta tgg ctg cag cag  cta gaa gaa aaa ggc  cga tac      4666
Asp Ala Arg  Leu Trp Leu Gln Gln  Leu Glu Glu Lys Gly  Arg Tyr
        1030                1035                1040

gca aaa gac  gtg tgg gct ggg taa attaaaaaga ggctaggata aaagtagttt  4720
Ala Lys Asp  Val Trp Ala Gly
        1045

agttggttga aggaagatcc gaacgatgaa tcgttcggat ctttttattg gtagagtaaa  4780

cgtagatttc atctatttag tgacttgtag cggttgattg gagggcaagg tgaagactcc  4840

aatcaaccgc ggtgtcacat gcaagccata cgaaattcat ttctcccatt tattcgtctt  4900

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Ile Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Arg
        35                  40                  45

Val Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp
    50                  55                  60

Glu Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Phe Val Arg
65                  70                  75                  80

Asp Phe Ala Gly Asp Gly Leu Phe Thr Ser Trp Thr His Glu Lys Asn
                85                  90                  95

Trp Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala
            100                 105                 110

Met Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val
        115                 120                 125

Gln Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Pro Glu
    130                 135                 140

Asp Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn
145                 150                 155                 160

Tyr Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Thr
                165                 170                 175

Ser Met Val Arg Ala Leu Asp Glu Ala Met Asn Lys Leu Gln Arg Ala
            180                 185                 190

Asn Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Phe Gln Glu
        195                 200                 205

Asp Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg
    210                 215                 220

Lys Ala Ser Gly Glu Gln Ser Asp Asp Leu Leu Thr His Met Leu Asn
225                 230                 235                 240

Gly Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Glu Asn Ile Arg
                245                 250                 255
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Tyr Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly
260 265 270

Leu Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu
275 280 285

Gln Lys Ala Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro
290 295 300

Ser Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn
305 310 315 320

Glu Ala Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala
325 330 335

Lys Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp
340 345 350

Glu Leu Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp
355 360 365

Gly Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser
370 375 380

Ala Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala
385 390 395 400

Cys Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly
405 410 415

Met Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu
420 425 430

Asp Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys
435 440 445

Ala Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr
450 455 460

Glu Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn
465 470 475 480

Thr Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly
485 490 495

Thr Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro
500 505 510

Gln Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly
515 520 525

Ala Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn
530 535 540

Ala Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val
545 550 555 560

Lys Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala
565 570 575

Thr Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala
580 585 590

Lys Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp
595 600 605

Asp Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp
610 615 620

Val Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys
625 630 635 640

Ser Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu
645 650 655

Ala Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu

660 665 670

Leu Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu
675 680 685

Leu Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile
690 695 700

Pro Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly
705 710 715 720

Leu Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu
725 730 735

Ala His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln
740 745 750

Tyr Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met
755 760 765

Ala Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu
770 775 780

Leu Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr
785 790 795 800

Met Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser
805 810 815

Glu Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile
820 825 830

Ser Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser
835 840 845

Val Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile
850 855 860

Ala Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys
865 870 875 880

Phe Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu
885 890 895

Thr Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg
900 905 910

Gly Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu
915 920 925

Gly Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr
930 935 940

Leu Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr
945 950 955 960

Leu His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val
965 970 975

Gln His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp
980 985 990

Gln Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro
995 1000 1005

Ala Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln
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1               5                  10                  15

tta ccg tta tta aac aca gat aaa ccg gtt caa gct ttg atg aaa att        96
Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
            20                  25                  30

gcg gat gaa tta gga gaa atc ttt aaa ttc gag gcg cct ggt cgt gta       144
Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Arg Val
        35                  40                  45

acg cgc tac tta tca agt cag cgt cta att aaa gaa gca tgc gat gaa       192
Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
    50                  55                  60

tca cgc ttt gat aaa aac tta agt caa gcg ctt aaa ttt gta cgt gat       240
Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Phe Val Arg Asp
65                  70                  75                  80

ttt gca gga gac ggg tta gct aca agc tgg acg cat gaa aaa aat tgg       288
Phe Ala Gly Asp Gly Leu Ala Thr Ser Trp Thr His Glu Lys Asn Trp
                85                  90                  95

aaa aaa gcg cat aat atc tta ctt cca agc ttc agt cag cag gca atg       336
Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
            100                 105                 110

aaa ggc tat cat gcg atg atg gtc gat atc gcc gtg cag ctt gtt caa       384
Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
        115                 120                 125

aag tgg gag cgt cta aat gca gat gag cat att gaa gta ccg gaa gac       432
Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Pro Glu Asp
    130                 135                 140

atg aca cgt tta acg ctt gat aca att ggt ctt tgc ggc ttt aac tat       480
Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
145                 150                 155                 160

cgc ttt aac agc ttt tac cga gat cag cct cat cca ttt att aca agt       528
Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Thr Ser
                165                 170                 175

atg gtc cgt gca ctg gat gaa gca atg aac aag ctg cag cga gca aat       576
Met Val Arg Ala Leu Asp Glu Ala Met Asn Lys Leu Gln Arg Ala Asn
            180                 185                 190

cca gac gac cca gct tat gat gaa aac aag cgc cag ttt caa gaa gat       624
Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Phe Gln Glu Asp
        195                 200                 205

atc aag gtg atg aac gac cta gta gat aaa att att gca gat cgc aaa       672
Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
    210                 215                 220

gca agc ggt gaa caa agc gat gat tta tta acg cat atg cta aac gga       720
Ala Ser Gly Glu Gln Ser Asp Asp Leu Leu Thr His Met Leu Asn Gly
225                 230                 235                 240

aaa gat cca gaa acg ggt gag ccg ctt gat gac gag aac att cgc tat       768
Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Glu Asn Ile Arg Tyr
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                    245                 250                 255

caa att att aca ttc tta att gcg gga cac gaa aca aca agt ggt ctt      816
Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
            260                 265                 270

tta tca ttt gcg ctg tat ttc tta gtg aaa aat cca cat gta tta caa      864
Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
        275                 280                 285

aaa gca gca gaa gaa gca gca cga gtt cta gta gat cct gtt cca agc      912
Lys Ala Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
    290                 295                 300

tac aaa caa gtc aaa cag ctt aaa tat gtc ggc atg gtc tta aac gaa      960
Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
305                 310                 315                 320

gcg ctg cgc tta tgg cca act gct cct gcg ttt tcc cta tat gca aaa     1008
Ala Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala Lys
                325                 330                 335

gaa gat acg gtg ctt gga gga gaa tat cct tta gaa aaa ggc gac gaa     1056
Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
            340                 345                 350

cta atg gtt ctg att cct cag ctt cac cgt gat aaa aca att tgg gga     1104
Leu Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
        355                 360                 365

gac gat gtg gaa gag ttc cgt cca gag cgt ttt gaa aat cca agt gcg     1152
Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
    370                 375                 380

att ccg cag cat gcg ttt aaa ccg ttt gga aac ggt cag cgt gcg tgt     1200
Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385                 390                 395                 400

atc ggt cag cag ttc gct ctt cat gaa gca acg ctg gta ctt ggt atg     1248
Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
                405                 410                 415

atg cta aaa cac ttt gac ttt gaa gat cat aca aac tac gag ctg gat     1296
Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
            420                 425                 430

att aaa gaa act tta acg tta aaa cct gaa ggc ttt gtg gta aaa gca     1344
Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
        435                 440                 445

aaa tcg aaa aaa att ccg ctt ggc ggt att cct tca cct agc act gaa     1392
Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
    450                 455                 460

cag tct gct aaa aaa gta cgc aaa aag gca gaa aac gct cat aat acg     1440
Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
465                 470                 475                 480

ccg ctg ctt gtg cta tac ggt tca aat atg gga aca gct gaa gga acg     1488
Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
                485                 490                 495

gcg cgt gat tta gca gat att gca atg agc aaa gga ttt gca ccg cag     1536
Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
            500                 505                 510

gtc gca acg ctt gat tca cac gcc gga aat ctt ccg cgc gaa gga gct     1584
Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
        515                 520                 525

gta tta att gta acg gcg tct tat aac ggt cat ccg cct gat aac gca     1632
Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
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aag caa ttt gtc gac tgg tta gac caa gcg tct gct gat gaa gta aaa     1680
Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
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545                 550                 555                 560

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acg tat caa aaa gtg cct gct ttt atc gat gaa acg ctt gcc gct aaa      1776
Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
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ggg gca gaa aac atc gct gac cgc ggt gaa gca gat gca agc gac gac      1824
Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
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ttt gaa ggc aca tat gaa gaa tgg cgt gaa cat atg tgg agt gac gta      1872
Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
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gca gcc tac ttt aac ctc gac att gaa aac agt gaa gat aat aaa tct      1920
Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
625                 630                 635                 640

act ctt tca ctt caa ttt gtc gac agc gcc gcg gat atg ccg ctt gcg      1968
Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
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aaa atg cac ggt gcg ttt tca acg aac gtc gta gca agc aaa gaa ctt      2016
Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
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caa cag cca ggc agt gca cga agc acg cga cat ctt gaa att gaa ctt      2064
Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
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cca aaa gaa gct tct tat caa gaa gga gat cat tta ggt gtt att cct      2112
Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
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cgc aac tat gaa gga ata gta aac cgt gta aca gca agg ttc ggc cta      2160
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705                 710                 715                 720

gat gca tca cag caa atc cgt ctg gaa gca gaa gaa gaa aaa tta gct      2208
Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
                725                 730                 735

cat ttg cca ctc gct aaa aca gta tcc gta gaa gag ctt ctg caa tac      2256
His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
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gtg gag ctt caa gat cct gtt acg cgc acg cag ctt cgc gca atg gct      2304
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        755                 760                 765

gct aaa acg gtc tgc ccg ccg cat aaa gta gag ctt gaa gcc ttg ctt      2352
Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
    770                 775                 780

gaa aag caa gcc tac aaa gaa caa gtg ctg gca aaa cgt tta aca atg      2400
Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785                 790                 795                 800

ctt gaa ctg ctt gaa aaa tac ccg gcg tgt gaa atg aaa ttc agc gaa      2448
Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
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Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
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tca tca cct cgt gtc gat gaa aaa caa gca agc atc acg gtc agc gtt      2544
Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
        835                 840                 845

gtc tca gga gaa gcg tgg agc gga tat gga gaa tat aaa gga att gcg      2592
Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
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Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
                885                 890                 895

ccg ctt atc atg gtc gga ccg gga aca ggc gtc gcg ccg ttt aga ggc      2736
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ttt gtg cag gcg cgc aaa cag cta aaa gaa caa gga cag tca ctt gga      2784
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Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
    930                 935                 940

tat caa gaa gag ctt gaa aac gcc caa agc gaa ggc atc att acg ctt      2880
Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
945                 950                 955                 960

cat acc gct ttt tct cgc atg cca aat cag ccg aaa aca tac gtt cag      2928
His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
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cac gta atg gaa caa gac ggc aag aaa ttg att gaa ctt ctt gat caa      2976
His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
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gga gcg cac ttc tat att tgc gga  gac gga agc caa atg  gca cct gcc    3024
Gly Ala His Phe Tyr Ile Cys Gly  Asp Gly Ser Gln Met  Ala Pro Ala
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gtt gaa  gca acg ctt atg aaa  agc tat gct gac gtt  cac caa gtg       3069
Val Glu  Ala Thr Leu Met Lys  Ser Tyr Ala Asp Val  His Gln Val
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agt gaa  gca gac gct cgc tta  tgg ctg cag cag cta  gaa gaa aaa       3114
Ser Glu  Ala Asp Ala Arg Leu  Trp Leu Gln Gln Leu  Glu Glu Lys
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Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
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Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Phe Val Arg Asp
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Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
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Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
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Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Pro Glu Asp
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Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
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Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Thr Ser
165 170 175

Met Val Arg Ala Leu Asp Glu Ala Met Asn Lys Leu Gln Arg Ala Asn
180 185 190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Phe Gln Glu Asp
195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
210 215 220

Ala Ser Gly Glu Gln Ser Asp Asp Leu Leu Thr His Met Leu Asn Gly
225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Glu Asn Ile Arg Tyr
245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
275 280 285

Lys Ala Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
340 345 350

Leu Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
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Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
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Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
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Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr

485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
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Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
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Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
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Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
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Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
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Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
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Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
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Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
690 695 700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
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Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
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Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
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Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
20 25 30

gcg gat gaa tta gga gaa atc ttt aaa ttc gag gcg cct ggt cgt gta 144
Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Arg Val
35 40 45

acg cgc tac tta tca agt cag cgt cta att aaa gaa gca tgc gat gaa 192
Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
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Ser Arg Phe Asp Lys Asn Leu Ser Gln Gly Leu Lys Phe Val Arg Asp
65 70 75 80

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85 90 95

aaa aaa gcg cat aat atc tta ctt cca agc ttc agt cag cag gca atg 336
Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
100 105 110

aaa ggc tat cat gcg atg atg gtc gat atc gcc gtg cag ctt gtt caa 384

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Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Pro Glu Asp
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Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
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cgc ttt aac agc ttt tac cga gat cag cct cat cca ttt att aca agt      528
Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Thr Ser
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atg gtc cgt gca ctg gat gaa gca atg aac aag cag cag cga gca aat      576
Met Val Arg Ala Leu Asp Glu Ala Met Asn Lys Gln Gln Arg Ala Asn
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cca gac gac cca gct tat gat gaa aac aag cgc cag ttt caa gaa gat      624
Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Phe Gln Glu Asp
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atc aag gtg atg aac gac cta gta gat aaa att att gca gat cgc aaa      672
Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
    210                 215                 220

gca agc ggt gaa caa agc gat gat tta tta acg cat atg cta aac gga      720
Ala Ser Gly Glu Gln Ser Asp Asp Leu Leu Thr His Met Leu Asn Gly
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Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Glu Asn Ile Arg Tyr
                245                 250                 255

caa att att aca ttc tta att gcg gga cac gaa aca aca agt ggt ctt      816
Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
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tta tca ttt gcg ctg tat ttc tta gtg aaa aat cca cat gta tta caa      864
Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
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aaa gca gca gaa gaa gca gca cga gtt cta gta gat cct gtt cca agc      912
Lys Ala Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
    290                 295                 300

tac aaa caa gtc aaa cag ctt aaa tat gtc ggc atg gtc tta aac gaa      960
Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
305                 310                 315                 320

gcg ctg cgc tta tgg cca act gct cct gcg ttt tcc cta tat gca aaa     1008
Ala Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala Lys
                325                 330                 335

gaa gat acg gtg ctt gga gga gaa tat cct tta gaa aaa ggc gac gaa     1056
Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
            340                 345                 350

cta atg gtt ctg att cct cag ctt cac cgt gat aaa aca att tgg gga     1104
Leu Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
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atc ggt cag cag ttc gct ctt cat gaa gca acg ctg gta ctt ggt atg     1248
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cag tct gct aaa aaa gta cgc aaa aag gca gaa aac gct cat aat acg     1440
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465                 470                 475                 480

ccg ctg ctt gtg cta tac ggt tca aat atg gga aca gct gaa gga acg     1488
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gcg cgt gat tta gca gat att gca atg agc aaa gga ttt gca ccg cag     1536
Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
            500                 505                 510

gtc gca acg ctt gat tca cac gcc gga aat ctt ccg cgc gaa gga gct     1584
Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
        515                 520                 525

gta tta att gta acg gcg tct tat aac ggt cat ccg cct gat aac gca     1632
Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
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aag caa ttt gtc gac tgg tta gac caa gcg tct gct gat gaa gta aaa     1680
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Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
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ggg gca gaa aac atc gct gac cgc ggt gaa gca gat gca agc gac gac     1824
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gca gcc tac ttt aac ctc gac att gaa aac agt gaa gat aat aaa tct     1920
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625                 630                 635                 640

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caa cag cca ggc agt gca cga agc acg cga cat ctt gaa att gaa ctt     2064
Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
        675                 680                 685

cca aaa gaa gct tct tat caa gaa gga gat cat tta ggt gtt att cct     2112
Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
    690                 695                 700

cgc aac tat gaa gga ata gta aac cgt gta aca gca agg ttc ggc cta     2160
Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
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gtg gag ctt caa gat cct gtt acg cgc acg cag ctt cgc gca atg gct      2304
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        755                 760                 765

gct aaa acg gtc tgc ccg ccg cat aaa gta gag ctt gaa gcc ttg ctt      2352
Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
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gaa aag caa gcc tac aaa gaa caa gtg ctg gca aaa cgt tta aca atg      2400
Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785                 790                 795                 800

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gtc tca gga gaa gcg tgg agc gga tat gga gaa tat aaa gga att gcg      2592
Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
    850                 855                 860

tcg aac tat ctt gcc gag ctg caa gaa gga gat acg att acg tgc ttt      2640
Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865                 870                 875                 880

att tcc aca ccg cag tca gaa ttt acg ctg cca aaa gac cct gaa acg      2688
Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
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Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
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gaa gca cat tta tac ttc ggc tgc cgt tca cct cat gaa gac tat ctg      2832
Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
    930                 935                 940

tat caa gaa gag ctt gaa aac gcc caa agc gaa ggc atc att acg ctt      2880
Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
945                 950                 955                 960

cat acc gct ttt tct cgc atg cca aat cag ccg aaa aca tac gtt cag      2928
His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
                965                 970                 975

cac gta atg gaa caa gac ggc aag aaa ttg att gaa ctt ctt gat caa      2976
His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
            980                 985                 990

gga gcg cac ttc tat att tgc gga  gac gga agc caa atg  gca cct gcc    3024
Gly Ala His Phe Tyr Ile Cys Gly  Asp Gly Ser Gln Met  Ala Pro Ala
        995                 1000                1005

gtt gaa  gca acg ctt atg aaa  agc tat gct gac gtt  cac caa gtg       3069
Val Glu  Ala Thr Leu Met Lys  Ser Tyr Ala Asp Val  His Gln Val
    1010                1015                1020

agt gaa  gca gac gct cgc tta  tgg ctg cag cag cta  gaa gaa aaa       3114
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Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
1025 1030 1035

ggc cga tac gca aaa gac gtg tgg gct ggg taa 3147
Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
1040 1045

<210> 8
<211> 1048
<212> PRT
<213> Artificial sequence

<220>
<223> Cytochrome P450BM-3 mutant

<400> 8

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Arg Val
35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Gly Leu Lys Phe Val Arg Asp
65 70 75 80

Phe Ala Gly Asp Gly Leu Val Thr Ser Trp Thr His Glu Lys Asn Trp
85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Pro Glu Asp
130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Thr Ser
165 170 175

Met Val Arg Ala Leu Asp Glu Ala Met Asn Lys Gln Gln Arg Ala Asn
180 185 190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Phe Gln Glu Asp
195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
210 215 220

Ala Ser Gly Glu Gln Ser Asp Asp Leu Leu Thr His Met Leu Asn Gly
225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Glu Asn Ile Arg Tyr
245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
275 280 285

Lys Ala Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
340 345 350

Leu Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
690 695 700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu

705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
1040 1045

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<211> 1032
<212> DNA
<213> Nocardia corallina

<220>
<221> CDS
<222> (1)..(1032)

<400> 9

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atg acg aca gag gcg acg gtg gcc cga ccg gtg gag ctc gaa ggt cac        48
Met Thr Thr Glu Ala Thr Val Ala Arg Pro Val Glu Leu Glu Gly His
1               5                  10                  15

cgg aca ttc acc tgg ttc acg ccc gcc agg cga aag ccg acg gag tac        96
Arg Thr Phe Thr Trp Phe Thr Pro Ala Arg Arg Lys Pro Thr Glu Tyr
            20                  25                  30

gag ctc tac acc gtg ggt caa cag tcc act ccg gac gag tgg ctg cat       144
Glu Leu Tyr Thr Val Gly Gln Gln Ser Thr Pro Asp Glu Trp Leu His
        35                  40                  45

gtg gac tgg ccg ctg cgc ttc gac gac ggc cgc gcc ccg tgg gag gag       192
Val Asp Trp Pro Leu Arg Phe Asp Asp Gly Arg Ala Pro Trp Glu Glu
    50                  55                  60

gag tcg agt gcg gta cgg acc tcg gag tgg tcg gct tac cgc gac cca       240
Glu Ser Ser Ala Val Arg Thr Ser Glu Trp Ser Ala Tyr Arg Asp Pro
65                  70                  75                  80

cac caa ctg tgg cag cgt ccc tac gtc agc acg tgc aac cag gac cag       288
His Gln Leu Trp Gln Arg Pro Tyr Val Ser Thr Cys Asn Gln Asp Gln
                85                  90                  95

cag gcc ctc gcg cgg ctg gtc ccc gtc ctg acc atg ggg tcg gcg gcg       336
Gln Ala Leu Ala Arg Leu Val Pro Val Leu Thr Met Gly Ser Ala Ala
            100                 105                 110

atc acg ccc atc tgg tcg cag aag atc ctc gcc agg tcc tac gcc gcc       384
Ile Thr Pro Ile Trp Ser Gln Lys Ile Leu Ala Arg Ser Tyr Ala Ala
        115                 120                 125

tgg cca ttc gtc gag tac ggg ctc ttc ctg agc ctg gcc tac gcc gtg       432
Trp Pro Phe Val Glu Tyr Gly Leu Phe Leu Ser Leu Ala Tyr Ala Val
    130                 135                 140

cgc cag gcc atg tcc gac acg gtc cag ttc agc gtg gtg ttc cag gcc       480
Arg Gln Ala Met Ser Asp Thr Val Gln Phe Ser Val Val Phe Gln Ala
145                 150                 155                 160

gtg gac cgc atg cgg ctg ctc cag gac atc gtc cac cac ctg gac cac       528
Val Asp Arg Met Arg Leu Leu Gln Asp Ile Val His His Leu Asp His
                165                 170                 175

ctg cag gag tcg ccg gaa ttc agc gac gcc ggg gcc cgc gag gcc tgg       576
Leu Gln Glu Ser Pro Glu Phe Ser Asp Ala Gly Ala Arg Glu Ala Trp
            180                 185                 190

atg tcc gac tcc acc ctg gtc ccg atc cgg gaa gtg atc gag cgc atc       624
Met Ser Asp Ser Thr Leu Val Pro Ile Arg Glu Val Ile Glu Arg Ile
        195                 200                 205

gcc gcc agc cag gac tgg gtg gag atc ctg gtc gcc ggc acg ctc gtc       672
Ala Ala Ser Gln Asp Trp Val Glu Ile Leu Val Ala Gly Thr Leu Val
    210                 215                 220

ttc gag cct ctg gtc ggc cac ctg gcg aag gcc gag ttg ttc agc cgc       720
Phe Glu Pro Leu Val Gly His Leu Ala Lys Ala Glu Leu Phe Ser Arg
225                 230                 235                 240

cgt gcg cca atg ttc ggg gac ggg acc acg ccg gcg gtg ctg gcg tcg       768
Arg Ala Pro Met Phe Gly Asp Gly Thr Thr Pro Ala Val Leu Ala Ser
                245                 250                 255

gcc ctg ctg gac agc ggc agg cac ctc gaa tcg gtc cag gcg ctc gtc       816
Ala Leu Leu Asp Ser Gly Arg His Leu Glu Ser Val Gln Ala Leu Val
            260                 265                 270

cgc ctc gtc tgc caa gac ccc gtc cat ggc gac cag aac cag gcg act       864
Arg Leu Val Cys Gln Asp Pro Val His Gly Asp Gln Asn Gln Ala Thr
        275                 280                 285

gtg cgg cgg tgg atc gag gaa tgg cag ccg cgg tgc aag gcg gcg gcc       912
Val Arg Arg Trp Ile Glu Glu Trp Gln Pro Arg Cys Lys Ala Ala Ala
    290                 295                 300
```

```
cag tcc ttc ctg ccg acg ttc tcc gac tgc ggc atc gac gcc aag gaa      960
Gln Ser Phe Leu Pro Thr Phe Ser Asp Cys Gly Ile Asp Ala Lys Glu
305                 310                 315                 320

agc gcc aac gcg ctg tcc cgg gcg ctg gcg aac cag cgg gcc gcc gtc     1008
Ser Ala Asn Ala Leu Ser Arg Ala Leu Ala Asn Gln Arg Ala Ala Val
                325                 330                 335

gag ggc gcc ggc atc acg gca tga                                    1032
Glu Gly Ala Gly Ile Thr Ala
            340
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<210> 10
<211> 343
<212> PRT
<213> Nocardia corallina

<400> 10

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Met Thr Thr Glu Ala Thr Val Ala Arg Pro Val Glu Leu Glu Gly His
1               5                  10                  15

Arg Thr Phe Thr Trp Phe Thr Pro Ala Arg Arg Lys Pro Thr Glu Tyr
            20                  25                  30

Glu Leu Tyr Thr Val Gly Gln Gln Ser Thr Pro Asp Glu Trp Leu His
        35                  40                  45

Val Asp Trp Pro Leu Arg Phe Asp Asp Gly Arg Ala Pro Trp Glu Glu
    50                  55                  60

Glu Ser Ser Ala Val Arg Thr Ser Glu Trp Ser Ala Tyr Arg Asp Pro
65                  70                  75                  80

His Gln Leu Trp Gln Arg Pro Tyr Val Ser Thr Cys Asn Gln Asp Gln
                85                  90                  95

Gln Ala Leu Ala Arg Leu Val Pro Val Leu Thr Met Gly Ser Ala Ala
            100                 105                 110

Ile Thr Pro Ile Trp Ser Gln Lys Ile Leu Ala Arg Ser Tyr Ala Ala
        115                 120                 125

Trp Pro Phe Val Glu Tyr Gly Leu Phe Leu Ser Leu Ala Tyr Ala Val
    130                 135                 140

Arg Gln Ala Met Ser Asp Thr Val Gln Phe Ser Val Val Phe Gln Ala
145                 150                 155                 160

Val Asp Arg Met Arg Leu Leu Gln Asp Ile Val His His Leu Asp His
                165                 170                 175

Leu Gln Glu Ser Pro Glu Phe Ser Asp Ala Gly Ala Arg Glu Ala Trp
            180                 185                 190

Met Ser Asp Ser Thr Leu Val Pro Ile Arg Glu Val Ile Glu Arg Ile
        195                 200                 205

Ala Ala Ser Gln Asp Trp Val Glu Ile Leu Val Ala Gly Thr Leu Val
    210                 215                 220

Phe Glu Pro Leu Val Gly His Leu Ala Lys Ala Glu Leu Phe Ser Arg
225                 230                 235                 240

Arg Ala Pro Met Phe Gly Asp Gly Thr Thr Pro Ala Val Leu Ala Ser
                245                 250                 255

Ala Leu Leu Asp Ser Gly Arg His Leu Glu Ser Val Gln Ala Leu Val
            260                 265                 270

Arg Leu Val Cys Gln Asp Pro Val His Gly Asp Gln Asn Gln Ala Thr
        275                 280                 285

Val Arg Arg Trp Ile Glu Glu Trp Gln Pro Arg Cys Lys Ala Ala Ala
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290 295 300

Gln Ser Phe Leu Pro Thr Phe Ser Asp Cys Gly Ile Asp Ala Lys Glu
305 310 315 320

Ser Ala Asn Ala Leu Ser Arg Ala Leu Ala Asn Gln Arg Ala Ala Val
325 330 335

Glu Gly Ala Gly Ile Thr Ala
340

<210> 11
<211> 1506
<212> DNA
<213> Nocardia corallina

<220>
<221> CDS
<222> (1)..(1506)

<400> 11

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atg gca tcg aac ccc acc cag ctc cac gag aag tcg aag tcc tac gac      48
Met Ala Ser Asn Pro Thr Gln Leu His Glu Lys Ser Lys Ser Tyr Asp
1               5                  10                  15

tgg gac ttc acc tcc gtc gag cgg cgc ccc aag ttc gag acg aag tac      96
Trp Asp Phe Thr Ser Val Glu Arg Arg Pro Lys Phe Glu Thr Lys Tyr
            20                  25                  30

aag atg ccc aag aag ggc aag gac ccg ttc cgc gtc ctg atc cgt gac     144
Lys Met Pro Lys Lys Gly Lys Asp Pro Phe Arg Val Leu Ile Arg Asp
        35                  40                  45

tac atg aag atg gaa gcg gag aag gac gac cgg acc cat ggc ttc ctc     192
Tyr Met Lys Met Glu Ala Glu Lys Asp Asp Arg Thr His Gly Phe Leu
    50                  55                  60

gac ggc gcc gtg cgg acg cgt gag gcc acc agg att gag ccg cgg ttc     240
Asp Gly Ala Val Arg Thr Arg Glu Ala Thr Arg Ile Glu Pro Arg Phe
65                  70                  75                  80

gct gag gcc atg aag atc atg gtg ccg cag ctg acc aac gcc gag tac     288
Ala Glu Ala Met Lys Ile Met Val Pro Gln Leu Thr Asn Ala Glu Tyr
                85                  90                  95

cag gcg gtg gcg ggc tgc gga atg atc atc tcg gcc gtc gag aac cag     336
Gln Ala Val Ala Gly Cys Gly Met Ile Ile Ser Ala Val Glu Asn Gln
            100                 105                 110

gag ctc cgt cag ggc tac gcc gct cag atg ctc gat gag gtg cgg cac     384
Glu Leu Arg Gln Gly Tyr Ala Ala Gln Met Leu Asp Glu Val Arg His
        115                 120                 125

gcg cag ctc gag atg acg cta cgc aac tac tac gcg aag cac tgg tgc     432
Ala Gln Leu Glu Met Thr Leu Arg Asn Tyr Tyr Ala Lys His Trp Cys
    130                 135                 140

gat ccc tcc ggc ttc gac atc ggt cag cgc ggc ctg tac cag cac ccc     480
Asp Pro Ser Gly Phe Asp Ile Gly Gln Arg Gly Leu Tyr Gln His Pro
145                 150                 155                 160

gcg ggg ctg gtg tcc atc ggc gag ttc cag cac ttc aat act ggt gac     528
Ala Gly Leu Val Ser Ile Gly Glu Phe Gln His Phe Asn Thr Gly Asp
                165                 170                 175

ccg ctt gac gtc atc atc gat ctc aac atc gtg gcc gag acg gcg ttc     576
Pro Leu Asp Val Ile Ile Asp Leu Asn Ile Val Ala Glu Thr Ala Phe
            180                 185                 190

acg aac atc ctg ctg gtg gcc act cca cag gtc gcc gtg gcc aac ggg     624
Thr Asn Ile Leu Leu Val Ala Thr Pro Gln Val Ala Val Ala Asn Gly
        195                 200                 205

gac aac gcg atg gcc agc gtg ttc ctc tcg atc cag tcg gac gag gcc     672
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Asp Asn Ala Met Ala Ser Val Phe Leu Ser Ile Gln Ser Asp Glu Ala
    210                 215                 220

agg cac atg gcc aac ggg tac ggc tcg gtc atg gcg ctg ctg gag aac      720
Arg His Met Ala Asn Gly Tyr Gly Ser Val Met Ala Leu Leu Glu Asn
225                 230                 235                 240

gag gac aac ctc ccg ctg ctc aac cag tct ctc gat cgg cac ttc tgg      768
Glu Asp Asn Leu Pro Leu Leu Asn Gln Ser Leu Asp Arg His Phe Trp
                245                 250                 255

cgt gcc cac aag gcc ttg gac aac gcg gtc gga tgg tgt tcg gag tat      816
Arg Ala His Lys Ala Leu Asp Asn Ala Val Gly Trp Cys Ser Glu Tyr
            260                 265                 270

ggc gcc cgc aag cgg cca tgg agc tac aag gcc cag tgg gag gaa tgg      864
Gly Ala Arg Lys Arg Pro Trp Ser Tyr Lys Ala Gln Trp Glu Glu Trp
        275                 280                 285

gtc gtc gac gac ttc gtg ggc ggc tac atc gac cga ctc agc gag ttc      912
Val Val Asp Asp Phe Val Gly Gly Tyr Ile Asp Arg Leu Ser Glu Phe
    290                 295                 300

ggc gtt cag gct ccg gcc tgc ctt ggc gcg gcc gcc gac gag gtc aag      960
Gly Val Gln Ala Pro Ala Cys Leu Gly Ala Ala Ala Asp Glu Val Lys
305                 310                 315                 320

tgg tcg cac cac acg ctc ggt cag gtg ctg tcg gcg gtg tgg ccg ctg     1008
Trp Ser His His Thr Leu Gly Gln Val Leu Ser Ala Val Trp Pro Leu
                325                 330                 335

aac ttc tgg cgc tcg gac gcc atg gga ccg gcg gac ttc gag tgg ttc     1056
Asn Phe Trp Arg Ser Asp Ala Met Gly Pro Ala Asp Phe Glu Trp Phe
            340                 345                 350

gag aac cac tac ccg ggc tgg agc gcg gcc tac cag ggt tac tgg gag     1104
Glu Asn His Tyr Pro Gly Trp Ser Ala Ala Tyr Gln Gly Tyr Trp Glu
        355                 360                 365

ggc tac aag gcg ctc gcc gac cca gca ggc gga cgc atc atg ctc cag     1152
Gly Tyr Lys Ala Leu Ala Asp Pro Ala Gly Gly Arg Ile Met Leu Gln
    370                 375                 380

gag ctg ccg ggt ctg ccg ccg atg tgt cag gtg tgc cag gtg ccg tgc     1200
Glu Leu Pro Gly Leu Pro Pro Met Cys Gln Val Cys Gln Val Pro Cys
385                 390                 395                 400

gtg atg ccg cgg ctg gat atg aac gcc gcg cgg atc atc gag ttc gag     1248
Val Met Pro Arg Leu Asp Met Asn Ala Ala Arg Ile Ile Glu Phe Glu
                405                 410                 415

ggg cag aaa atc gcg ctg tgc agc gaa ccc tgc cag cgg atc ttc acc     1296
Gly Gln Lys Ile Ala Leu Cys Ser Glu Pro Cys Gln Arg Ile Phe Thr
            420                 425                 430

aac tgg ccg gag gcg tac cgc cac cgc aag caa tac tgg gcc cgc tac     1344
Asn Trp Pro Glu Ala Tyr Arg His Arg Lys Gln Tyr Trp Ala Arg Tyr
        435                 440                 445

cac gga tgg gac ctg gcg gac gtc atc gtt gat ctc ggc tac atc cgc     1392
His Gly Trp Asp Leu Ala Asp Val Ile Val Asp Leu Gly Tyr Ile Arg
    450                 455                 460

ccg gac ggc aag acc ctc atc ggc cag ccg ctg ctc gag atg gag cgg     1440
Pro Asp Gly Lys Thr Leu Ile Gly Gln Pro Leu Leu Glu Met Glu Arg
465                 470                 475                 480

ctg tgg acc atc gac gac atc cgg gcc ctt cag tac gaa gtc aag gac     1488
Leu Trp Thr Ile Asp Asp Ile Arg Ala Leu Gln Tyr Glu Val Lys Asp
                485                 490                 495

ccg ttg cag gag gcg tga                                            1506
Pro Leu Gln Glu Ala
            500
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<210> 12
<211> 501
<212> PRT
<213> Nocardia corallina

<400> 12

Met Ala Ser Asn Pro Thr Gln Leu His Glu Lys Ser Lys Ser Tyr Asp
1 5 10 15

Trp Asp Phe Thr Ser Val Glu Arg Arg Pro Lys Phe Glu Thr Lys Tyr
20 25 30

Lys Met Pro Lys Lys Gly Lys Asp Pro Phe Arg Val Leu Ile Arg Asp
35 40 45

Tyr Met Lys Met Glu Ala Glu Lys Asp Asp Arg Thr His Gly Phe Leu
50 55 60

Asp Gly Ala Val Arg Thr Arg Glu Ala Thr Arg Ile Glu Pro Arg Phe
65 70 75 80

Ala Glu Ala Met Lys Ile Met Val Pro Gln Leu Thr Asn Ala Glu Tyr
85 90 95

Gln Ala Val Ala Gly Cys Gly Met Ile Ile Ser Ala Val Glu Asn Gln
100 105 110

Glu Leu Arg Gln Gly Tyr Ala Ala Gln Met Leu Asp Glu Val Arg His
115 120 125

Ala Gln Leu Glu Met Thr Leu Arg Asn Tyr Tyr Ala Lys His Trp Cys
130 135 140

Asp Pro Ser Gly Phe Asp Ile Gly Gln Arg Gly Leu Tyr Gln His Pro
145 150 155 160

Ala Gly Leu Val Ser Ile Gly Glu Phe Gln His Phe Asn Thr Gly Asp
165 170 175

Pro Leu Asp Val Ile Ile Asp Leu Asn Ile Val Ala Glu Thr Ala Phe
180 185 190

Thr Asn Ile Leu Leu Val Ala Thr Pro Gln Val Ala Val Ala Asn Gly
195 200 205

Asp Asn Ala Met Ala Ser Val Phe Leu Ser Ile Gln Ser Asp Glu Ala
210 215 220

Arg His Met Ala Asn Gly Tyr Gly Ser Val Met Ala Leu Leu Glu Asn
225 230 235 240

Glu Asp Asn Leu Pro Leu Leu Asn Gln Ser Leu Asp Arg His Phe Trp
245 250 255

Arg Ala His Lys Ala Leu Asp Asn Ala Val Gly Trp Cys Ser Glu Tyr
260 265 270

Gly Ala Arg Lys Arg Pro Trp Ser Tyr Lys Ala Gln Trp Glu Glu Trp
275 280 285

Val Val Asp Asp Phe Val Gly Gly Tyr Ile Asp Arg Leu Ser Glu Phe
290 295 300

Gly Val Gln Ala Pro Ala Cys Leu Gly Ala Ala Ala Asp Glu Val Lys
305 310 315 320

Trp Ser His His Thr Leu Gly Gln Val Leu Ser Ala Val Trp Pro Leu
325 330 335

Asn Phe Trp Arg Ser Asp Ala Met Gly Pro Ala Asp Phe Glu Trp Phe
340 345 350

Glu Asn His Tyr Pro Gly Trp Ser Ala Ala Tyr Gln Gly Tyr Trp Glu
355 360 365

Gly Tyr Lys Ala Leu Ala Asp Pro Ala Gly Gly Arg Ile Met Leu Gln
370 375 380

Glu Leu Pro Gly Leu Pro Pro Met Cys Gln Val Cys Gln Val Pro Cys
385 390 395 400

Val Met Pro Arg Leu Asp Met Asn Ala Ala Arg Ile Ile Glu Phe Glu
405 410 415

Gly Gln Lys Ile Ala Leu Cys Ser Glu Pro Cys Gln Arg Ile Phe Thr
420 425 430

Asn Trp Pro Glu Ala Tyr Arg His Arg Lys Gln Tyr Trp Ala Arg Tyr
435 440 445

His Gly Trp Asp Leu Ala Asp Val Ile Val Asp Leu Gly Tyr Ile Arg
450 455 460

Pro Asp Gly Lys Thr Leu Ile Gly Gln Pro Leu Leu Glu Met Glu Arg
465 470 475 480

Leu Trp Thr Ile Asp Asp Ile Arg Ala Leu Gln Tyr Glu Val Lys Asp
485 490 495

Pro Leu Gln Glu Ala
500

<210> 13
<211> 1494
<212> DNA
<213> Xanthobacta sp.

<220>
<221> CDS
<222> (1)..(1494)

<400> 13

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atg gcg ctc ttg aat cgg gac gat tgg tac gac atc gcg cgc gat gtc      48
Met Ala Leu Leu Asn Arg Asp Asp Trp Tyr Asp Ile Ala Arg Asp Val
1               5                  10                  15

gac tgg acg ctc agc tat gtc gac cgc gcg gtc gcc ttt ccc gag gag      96
Asp Trp Thr Leu Ser Tyr Val Asp Arg Ala Val Ala Phe Pro Glu Glu
            20                  25                  30

tgg aaa ggc gaa aag gac att tgc ggc acg gcc tgg gac gat tgg gac     144
Trp Lys Gly Glu Lys Asp Ile Cys Gly Thr Ala Trp Asp Asp Trp Asp
        35                  40                  45

gag ccc ttc cgg gtc tcc ttc cgc gaa tat gtg atg gtc cag cgc gac     192
Glu Pro Phe Arg Val Ser Phe Arg Glu Tyr Val Met Val Gln Arg Asp
    50                  55                  60

aag gaa gcg agc gtc ggc gcc atc cgc gag gcc atg gtc cgc gcc aag     240
Lys Glu Ala Ser Val Gly Ala Ile Arg Glu Ala Met Val Arg Ala Lys
65                  70                  75                  80

gcc tat gag aag ctc gac gac ggc cac aag gcc acc tcg cac ctg cac     288
Ala Tyr Glu Lys Leu Asp Asp Gly His Lys Ala Thr Ser His Leu His
                85                  90                  95

atg ggc acc atc acc atg gtg gag cac atg gcg gtc acc atg cag agc     336
Met Gly Thr Ile Thr Met Val Glu His Met Ala Val Thr Met Gln Ser
            100                 105                 110

cgg ttc gtg cgc ttc gcg ccg tcc gcc cgc tgg cgc agc ctc ggg gcg     384
Arg Phe Val Arg Phe Ala Pro Ser Ala Arg Trp Arg Ser Leu Gly Ala
        115                 120                 125

ttc ggc atg ctg gac gag acc cgc cac acc cag ctc gac ctg cgc ttc     432
Phe Gly Met Leu Asp Glu Thr Arg His Thr Gln Leu Asp Leu Arg Phe
    130                 135                 140

agc cac gat ctg ctc aac gat tcc ccg agc ttc gac tgg agc cag cgg     480
```

```
Ser His Asp Leu Leu Asn Asp Ser Pro Ser Phe Asp Trp Ser Gln Arg
145                 150                 155                 160

gcg ttc cac acc gac gaa tgg gcg gtt ctc gcc acc cgc aac ctg ttc      528
Ala Phe His Thr Asp Glu Trp Ala Val Leu Ala Thr Arg Asn Leu Phe
                165                 170                 175

gac gac atc atg ctc aac gcc gac tgc gtg gag gcg gcg ctc gcc acc      576
Asp Asp Ile Met Leu Asn Ala Asp Cys Val Glu Ala Ala Leu Ala Thr
            180                 185                 190

agc ctg acg ctg gag cac ggc ttc acc aac atc cag ttc gtg gcg ctc      624
Ser Leu Thr Leu Glu His Gly Phe Thr Asn Ile Gln Phe Val Ala Leu
        195                 200                 205

gcc tcc gac gcc atg gaa gcc ggc gac gtg aac ttc tcc aac ctc ttg      672
Ala Ser Asp Ala Met Glu Ala Gly Asp Val Asn Phe Ser Asn Leu Leu
    210                 215                 220

tcg agc atc cag acc gac gag gcg cgg cac gcc cag ttg ggc ttt ccc      720
Ser Ser Ile Gln Thr Asp Glu Ala Arg His Ala Gln Leu Gly Phe Pro
225                 230                 235                 240

acc ctc gac gtg atg atg aag cac gac ccc aag cgc gcc cag cag atc      768
Thr Leu Asp Val Met Met Lys His Asp Pro Lys Arg Ala Gln Gln Ile
                245                 250                 255

ctg gac gtc gcc ttc tgg cgc tcc tac cgc atc ttc cag gcg gtg acc      816
Leu Asp Val Ala Phe Trp Arg Ser Tyr Arg Ile Phe Gln Ala Val Thr
            260                 265                 270

ggc gtc tcc atg gac tac tac acg ccg gtc gcc aag cgg cag atg tcg      864
Gly Val Ser Met Asp Tyr Tyr Thr Pro Val Ala Lys Arg Gln Met Ser
        275                 280                 285

ttc aag gag ttc atg ctg gag tgg atc gtc aag cat cat gag cgc atc      912
Phe Lys Glu Phe Met Leu Glu Trp Ile Val Lys His His Glu Arg Ile
    290                 295                 300

ctg cgc gac tac ggc ctc cag aag ccc tgg tac tgg gac acg ttc gag      960
Leu Arg Asp Tyr Gly Leu Gln Lys Pro Trp Tyr Trp Asp Thr Phe Glu
305                 310                 315                 320

aag acc ctc gat cac ggc cac cac gcg ctg cac atc ggc acc tgg ttc     1008
Lys Thr Leu Asp His Gly His His Ala Leu His Ile Gly Thr Trp Phe
                325                 330                 335

tgg cgc ccg acc ctg ttc tgg gat ccc aat ggc ggc gtc tcg cgc gag     1056
Trp Arg Pro Thr Leu Phe Trp Asp Pro Asn Gly Gly Val Ser Arg Glu
            340                 345                 350

gag cgg cgc tgg ctg aac cag aag tat ccg aac tgg gaa gag agc tgg     1104
Glu Arg Arg Trp Leu Asn Gln Lys Tyr Pro Asn Trp Glu Glu Ser Trp
        355                 360                 365

ggc gtc ctg tgg gac gag atc atc tcc aac atc aat gcg ggc aac att     1152
Gly Val Leu Trp Asp Glu Ile Ile Ser Asn Ile Asn Ala Gly Asn Ile
    370                 375                 380

gaa aag acc ttg ccc gag acg ctg ccg atg ctg tgc aac gtc acc aac     1200
Glu Lys Thr Leu Pro Glu Thr Leu Pro Met Leu Cys Asn Val Thr Asn
385                 390                 395                 400

ctg ccc atc ggc tcg cac tgg gac cgc ttc cac ctg aag ccc gag cag     1248
Leu Pro Ile Gly Ser His Trp Asp Arg Phe His Leu Lys Pro Glu Gln
                405                 410                 415

ctc gtc tac aag ggg cgg ctc tac acc ttc gac agc gac gtc tcc aag     1296
Leu Val Tyr Lys Gly Arg Leu Tyr Thr Phe Asp Ser Asp Val Ser Lys
            420                 425                 430

tgg atc ttc gag ctc gat ccg gag cgc tat gcc ggc cac acc aac gtg     1344
Trp Ile Phe Glu Leu Asp Pro Glu Arg Tyr Ala Gly His Thr Asn Val
        435                 440                 445

gtc gac cgc ttc atc ggc ggg cag atc cag ccc atg acc atc gag ggc     1392
```

```
Val Asp Arg Phe Ile Gly Gly Gln Ile Gln Pro Met Thr Ile Glu Gly
    450                 455                 460

gtg ctc aac tgg atg ggc ctg acg ccc gaa gtc atg ggc aag gac gtg      1440
Val Leu Asn Trp Met Gly Leu Thr Pro Glu Val Met Gly Lys Asp Val
465                 470                 475                 480

ttc aac tac cgt tgg gcc ggc gat tac gcc gag aac cgg atc gcc gcc      1488
Phe Asn Tyr Arg Trp Ala Gly Asp Tyr Ala Glu Asn Arg Ile Ala Ala
                485                 490                 495

                                                                    1494
gag taa
Glu
```

<210> 14
<211> 497
<212> PRT
<213> Xanthobacta sp.

<400> 14

```
Met Ala Leu Leu Asn Arg Asp Asp Trp Tyr Asp Ile Ala Arg Asp Val
1               5                  10                  15

Asp Trp Thr Leu Ser Tyr Val Asp Arg Ala Val Ala Phe Pro Glu Glu
            20                  25                  30

Trp Lys Gly Glu Lys Asp Ile Cys Gly Thr Ala Trp Asp Asp Trp Asp
        35                  40                  45

Glu Pro Phe Arg Val Ser Phe Arg Glu Tyr Val Met Val Gln Arg Asp
    50                  55                  60

Lys Glu Ala Ser Val Gly Ala Ile Arg Glu Ala Met Val Arg Ala Lys
65                  70                  75                  80

Ala Tyr Glu Lys Leu Asp Asp Gly His Lys Ala Thr Ser His Leu His
                85                  90                  95

Met Gly Thr Ile Thr Met Val Glu His Met Ala Val Thr Met Gln Ser
            100                 105                 110

Arg Phe Val Arg Phe Ala Pro Ser Ala Arg Trp Arg Ser Leu Gly Ala
        115                 120                 125

Phe Gly Met Leu Asp Glu Thr Arg His Thr Gln Leu Asp Leu Arg Phe
    130                 135                 140

Ser His Asp Leu Leu Asn Asp Ser Pro Ser Phe Asp Trp Ser Gln Arg
145                 150                 155                 160

Ala Phe His Thr Asp Glu Trp Ala Val Leu Ala Thr Arg Asn Leu Phe
                165                 170                 175

Asp Asp Ile Met Leu Asn Ala Asp Cys Val Glu Ala Ala Leu Ala Thr
            180                 185                 190

Ser Leu Thr Leu Glu His Gly Phe Thr Asn Ile Gln Phe Val Ala Leu
        195                 200                 205

Ala Ser Asp Ala Met Glu Ala Gly Asp Val Asn Phe Ser Asn Leu Leu      210
215                 220

Ser Ser Ile Gln Thr Asp Glu Ala Arg His Ala Gln Leu Gly Phe Pro
225                 230                 235                 240

Thr Leu Asp Val Met Met Lys His Asp Pro Lys Arg Ala Gln Gln Ile
                245                 250                 255

Leu Asp Val Ala Phe Trp Arg Ser Tyr Arg Ile Phe Gln Ala Val Thr
            260                 265                 270

Gly Val Ser Met Asp Tyr Tyr Thr Pro Val Ala Lys Arg Gln Met Ser
        275                 280                 285
```

```
Phe Lys Glu Phe Met Leu Glu Trp Ile Val Lys His His Glu Arg Ile
    290                 295                 300

Leu Arg Asp Tyr Gly Leu Gln Lys Pro Trp Tyr Trp Asp Thr Phe Glu
305                 310                 315                 320

Lys Thr Leu Asp His Gly His His Ala Leu His Ile Gly Thr Trp Phe
                325                 330                 335

Trp Arg Pro Thr Leu Phe Trp Asp Pro Asn Gly Gly Val Ser Arg Glu
            340                 345                 350

Glu Arg Arg Trp Leu Asn Gln Lys Tyr Pro Asn Trp Glu Glu Ser Trp
        355                 360                 365

Gly Val Leu Trp Asp Glu Ile Ile Ser Asn Ile Asn Ala Gly Asn Ile
    370                 375                 380

Glu Lys Thr Leu Pro Glu Thr Leu Pro Met Leu Cys Asn Val Thr Asn
385                 390                 395                 400

Leu Pro Ile Gly Ser His Trp Asp Arg Phe His Leu Lys Pro Glu Gln
                405                 410                 415

Leu Val Tyr Lys Gly Arg Leu Tyr Thr Phe Asp Ser Asp Val Ser Lys
            420                 425                 430

Trp Ile Phe Glu Leu Asp Pro Glu Arg Tyr Ala Gly His Thr Asn Val
        435                 440                 445

Val Asp Arg Phe Ile Gly Gly Gln Ile Gln Pro Met Thr Ile Glu Gly
    450                 455                 460

Val Leu Asn Trp Met Gly Leu Thr Pro Glu Val Met Gly Lys Asp Val
465                 470                 475                 480

Phe Asn Tyr Arg Trp Ala Gly Asp Tyr Ala Glu Asn Arg Ile Ala Ala
                485                 490                 495

Glu
```

<210> 15
<211> 1026
<212> DNA
<213> Xanthobacta sp.

<220>
<221> CDS
<222> (1)..(1026)

<400> 15

```
atg aca cag cag cgc ccc acc cgc acg cgc gag cgc aag aag acc tgg      48
Met Thr Gln Gln Arg Pro Thr Arg Thr Arg Glu Arg Lys Lys Thr Trp
1               5                   10                  15

acg gct ttc ggc aat ctc gga cgc aag ccg acc gac tac gag gtc gtc      96
Thr Ala Phe Gly Asn Leu Gly Arg Lys Pro Thr Asp Tyr Glu Val Val
            20                  25                  30

acc cac aac atg aac cac acc atg cgc ggc acg ccc ctg gag ctg tcg     144
Thr His Asn Met Asn His Thr Met Arg Gly Thr Pro Leu Glu Leu Ser
        35                  40                  45

ccg acg gtg cac gcc aat gtg tgg ctc aag aag aac cgc gac gag atc     192
Pro Thr Val His Ala Asn Val Trp Leu Lys Lys Asn Arg Asp Glu Ile
    50                  55                  60

gcg ctc aag gtc gac agc tgg gat ctg ttc cgc gat ccc gac cgc acc     240
Ala Leu Lys Val Asp Ser Trp Asp Leu Phe Arg Asp Pro Asp Arg Thr
65                  70                  75                  80

acc tac gac acc tac gtc aag atg cag gac gac cag gag acc tat gtc     288
```

```
Thr Tyr Asp Thr Tyr Val Lys Met Gln Asp Asp Gln Glu Thr Tyr Val
                85                  90                  95

gac aac ctg ctc ctg tcc tac acc ggc gag ggc cgc tac gac gag gag   336
Asp Asn Leu Leu Leu Ser Tyr Thr Gly Glu Gly Arg Tyr Asp Glu Glu
            100                 105                 110

ctt tcc tcg cgc agc ctc gac ctc ctg tcc gcg ggg ctg acg ccg acc   384
Leu Ser Ser Arg Ser Leu Asp Leu Leu Ser Ala Gly Leu Thr Pro Thr
        115                 120                 125

cgc tat ctg ggc cat ggg ctg cag atg ctc gcg gcc tat atc cag cag   432
Arg Tyr Leu Gly His Gly Leu Gln Met Leu Ala Ala Tyr Ile Gln Gln
    130                 135                 140

ctc gcc ccg tcg gcc tat gtg ggc aat tgc gcg gtg ttc cag acc tcc   480
Leu Ala Pro Ser Ala Tyr Val Gly Asn Cys Ala Val Phe Gln Thr Ser
145                 150                 155                 160

gac gcg ctg cgc cgc gtg cag cgc gtc gcc tac cgc acc cgc cag ctc   528
Asp Ala Leu Arg Arg Val Gln Arg Val Ala Tyr Arg Thr Arg Gln Leu
                165                 170                 175

gcc gac gcc cat ccg gcc cgc ggc ttc ggc tcc ggc gac cgg gcg gtg   576
Ala Asp Ala His Pro Ala Arg Gly Phe Gly Ser Gly Asp Arg Ala Val
            180                 185                 190

tgg gag aag tcc ccg gac tgg cag ccc atc cgc aag gcc atc gag gag   624
Trp Glu Lys Ser Pro Asp Trp Gln Pro Ile Arg Lys Ala Ile Glu Glu
        195                 200                 205

ctg ctc gtc acc ttc gaa tgg gac aag gcg ctc gcc ggc acc aat ttc   672
Leu Leu Val Thr Phe Glu Trp Asp Lys Ala Leu Ala Gly Thr Asn Phe
    210                 215                 220

gtg gtg aag ccg atc ctc gac gag ctg ttc ctc aac cac ctg gcg cgc   720
Val Val Lys Pro Ile Leu Asp Glu Leu Phe Leu Asn His Leu Ala Arg
225                 230                 235                 240

ctg ctc cac gtg gag ggc gac gag ctc gac agc ctc gtg ctg cgg aac   768
Leu Leu His Val Glu Gly Asp Glu Leu Asp Ser Leu Val Leu Arg Asn
                245                 250                 255

ctt cac ggc gac gcc cag cgc cac gcc cgc tgg acg gcc gcg ctc ggc   816
Leu His Gly Asp Ala Gln Arg His Ala Arg Trp Thr Ala Ala Leu Gly
            260                 265                 270

cgc ttc gcc gtc gag cag aac gtg aac aac cgc acg gtc ctg cgc gac   864
Arg Phe Ala Val Glu Gln Asn Val Asn Asn Arg Thr Val Leu Arg Asp
        275                 280                 285

gcc atc gcc ggc tgg cac gag acc ggc gag gcg gtc ctc gcc gcg ggc   912
Ala Ile Ala Gly Trp His Glu Thr Gly Glu Ala Val Leu Ala Ala Gly
    290                 295                 300

gcc ggg atg ctt gcg agc cgc gcc ccc agc gcg gat gcg gcc aag atc   960
Ala Gly Met Leu Ala Ser Arg Ala Pro Ser Ala Asp Ala Ala Lys Ile
305                 310                 315                 320

gcc gac gag gtc cgc gcc acg ctc gcg cag ctg cac gcc aat gcg ggc  1008
Ala Asp Glu Val Arg Ala Thr Leu Ala Gln Leu His Ala Asn Ala Gly
                325                 330                 335

ctc ggg cac gat gcc tga                                         1026
Leu Gly His Asp Ala
            340
```

<210> 16
<211> 341
<212> PRT
<213> Xanthobacta sp.

<400> 16

Met Thr Gln Gln Arg Pro Thr Arg Thr Arg Glu Arg Lys Lys Thr Trp

```
1               5                   10                  15

Thr Ala Phe Gly Asn Leu Gly Arg Lys Pro Thr Asp Tyr Glu Val Val
            20                  25                  30

Thr His Asn Met Asn His Thr Met Arg Gly Thr Pro Leu Glu Leu Ser
        35                  40                  45

Pro Thr Val His Ala Asn Val Trp Leu Lys Lys Asn Arg Asp Glu Ile
    50                  55                  60

Ala Leu Lys Val Asp Ser Trp Asp Leu Phe Arg Asp Pro Asp Arg Thr
65                  70                  75                  80

Thr Tyr Asp Thr Tyr Val Lys Met Gln Asp Asp Gln Glu Thr Tyr Val
                85                  90                  95

Asp Asn Leu Leu Leu Ser Tyr Thr Gly Glu Gly Arg Tyr Asp Glu Glu
            100                 105                 110

Leu Ser Ser Arg Ser Leu Asp Leu Leu Ser Ala Gly Leu Thr Pro Thr
        115                 120                 125

Arg Tyr Leu Gly His Gly Leu Gln Met Leu Ala Ala Tyr Ile Gln Gln
    130                 135                 140

Leu Ala Pro Ser Ala Tyr Val Gly Asn Cys Ala Val Phe Gln Thr Ser
145                 150                 155                 160

Asp Ala Leu Arg Arg Val Gln Arg Val Ala Tyr Arg Thr Arg Gln Leu
                165                 170                 175

Ala Asp Ala His Pro Ala Arg Gly Phe Gly Ser Gly Asp Arg Ala Val
            180                 185                 190

Trp Glu Lys Ser Pro Asp Trp Gln Pro Ile Arg Lys Ala Ile Glu Glu
        195                 200                 205

Leu Leu Val Thr Phe Glu Trp Asp Lys Ala Leu Ala Gly Thr Asn Phe
    210                 215                 220

Val Val Lys Pro Ile Leu Asp Glu Leu Phe Leu Asn His Leu Ala Arg
225                 230                 235                 240

Leu Leu His Val Glu Gly Asp Glu Leu Asp Ser Leu Val Leu Arg Asn
                245                 250                 255

Leu His Gly Asp Ala Gln Arg His Ala Arg Trp Thr Ala Ala Leu Gly
            260                 265                 270

Arg Phe Ala Val Glu Gln Asn Val Asn Asn Arg Thr Val Leu Arg Asp
        275                 280                 285

Ala Ile Ala Gly Trp His Glu Thr Gly Glu Ala Val Leu Ala Ala Gly
    290                 295                 300

Ala Gly Met Leu Ala Ser Arg Ala Pro Ser Ala Asp Ala Ala Lys Ile
305                 310                 315                 320

Ala Asp Glu Val Arg Ala Thr Leu Ala Gln Leu His Ala Asn Ala Gly
                325                 330                 335

Leu Gly His Asp Ala
            340
```

<210> 17
<211> 267
<212> DNA
<213> Xanthobacta sp.

<220>
<221> CDS
<222> (1)..(267)

<400> 17
atg tct ttg ttc ccc atc gtg ggc cgc ttc gtg ggg gat ttc gtc ccc 48
Met Ser Leu Phe Pro Ile Val Gly Arg Phe Val Gly Asp Phe Val Pro
1 5 10 15

cac ctg gtg gcg gtg gac acc tct gac acc atc gat cag atc gcc gag 96
His Leu Val Ala Val Asp Thr Ser Asp Thr Ile Asp Gln Ile Ala Glu
20 25 30

aag gtg gcg gtc cac acg gtc ggg cgg cgc ttg ccg ccc gat ccc acc 144
Lys Val Ala Val His Thr Val Gly Arg Arg Leu Pro Pro Asp Pro Thr
35 40 45

gcc acc ggc tat gag gtg ctc ctc gac ggc gag acc ctg gac ggg ggc 192
Ala Thr Gly Tyr Glu Val Leu Leu Asp Gly Glu Thr Leu Asp Gly Gly
50 55 60

gcc acc ctg gag gcc atc atg acc aag cgc gag atg ctg ccc ctg cag 240
Ala Thr Leu Glu Ala Ile Met Thr Lys Arg Glu Met Leu Pro Leu Gln
65 70 75 80

tgg ttc gac gtg agg ttc aag aag tga 267
Trp Phe Asp Val Arg Phe Lys Lys
85

<210> 18
<211> 88
<212> PRT
<213> Xanthobacta sp.

<400> 18

Met Ser Leu Phe Pro Ile Val Gly Arg Phe Val Gly Asp Phe Val Pro
1 5 10 15

His Leu Val Ala Val Asp Thr Ser Asp Thr Ile Asp Gln Ile Ala Glu
20 25 30

Lys Val Ala Val His Thr Val Gly Arg Arg Leu Pro Pro Asp Pro Thr
35 40 45

Ala Thr Gly Tyr Glu Val Leu Leu Asp Gly Glu Thr Leu Asp Gly Gly
50 55 60

Ala Thr Leu Glu Ala Ile Met Thr Lys Arg Glu Met Leu Pro Leu Gln
65 70 75 80

Trp Phe Asp Val Arg Phe Lys Lys
85

<210> 19
<211> 1584
<212> DNA
<213> Methylococcus capsulatas

<220>
<221> CDS
<222> (1)..(1584)

<400> 19
atg gca ctt agc acc gca acc aag gcc gcg acg gac gcg ctg gct gcc 48
Met Ala Leu Ser Thr Ala Thr Lys Ala Ala Thr Asp Ala Leu Ala Ala
1 5 10 15

aat cgg gca ccc acc agc gtg aat gca cag gaa gtg cac cgt tgg ctc 96
Asn Arg Ala Pro Thr Ser Val Asn Ala Gln Glu Val His Arg Trp Leu
20 25 30

cag agc ttc aac tgg gat ttc aag aac aac cgg acc aag tac gcc acc 144
Gln Ser Phe Asn Trp Asp Phe Lys Asn Asn Arg Thr Lys Tyr Ala Thr
35 40 45

aag tac aag atg gcg aac gag acc aag gaa cag ttc aag ctg atc gcc 192

```
Lys Tyr Lys Met Ala Asn Glu Thr Lys Glu Gln Phe Lys Leu Ile Ala
    50                  55                  60

aag gaa tat gcg cgc atg gag gca gtc aag gac gaa agg cag ttc ggt      240
Lys Glu Tyr Ala Arg Met Glu Ala Val Lys Asp Glu Arg Gln Phe Gly
65                  70                  75                  80

agc ctg cag gat gcg ctg acc cgc ctc aac gcc ggt gtt cgc gtt cat      288
Ser Leu Gln Asp Ala Leu Thr Arg Leu Asn Ala Gly Val Arg Val His
                85                  90                  95

ccg aag tgg aac gag acc atg aaa gtg gtt tcg aac ttc ctg gaa gtg      336
Pro Lys Trp Asn Glu Thr Met Lys Val Val Ser Asn Phe Leu Glu Val
            100                 105                 110

ggc gaa tac aac gcc atc gcc gct acc ggg atg ctg tgg gat tcc gcc      384
Gly Glu Tyr Asn Ala Ile Ala Ala Thr Gly Met Leu Trp Asp Ser Ala
        115                 120                 125

cag gcg gcg gaa cag aag aac ggc tat ctg gcc cag gtg ttg gat gaa      432
Gln Ala Ala Glu Gln Lys Asn Gly Tyr Leu Ala Gln Val Leu Asp Glu
    130                 135                 140

atc cgc cac acc cac cag tgt gcc tac gtc aac tac tac ttc gcg aag      480
Ile Arg His Thr His Gln Cys Ala Tyr Val Asn Tyr Tyr Phe Ala Lys
145                 150                 155                 160

aac ggc cag gac ccg gcc ggt cac aac gat gct cgc cgc acc cgt acc      528
Asn Gly Gln Asp Pro Ala Gly His Asn Asp Ala Arg Arg Thr Arg Thr
                165                 170                 175

atc ggt ccg ctg tgg aag ggc atg aag cgc gtg ttt tcc gac ggc ttc      576
Ile Gly Pro Leu Trp Lys Gly Met Lys Arg Val Phe Ser Asp Gly Phe
            180                 185                 190

att tcc ggc gac gcc gtg gaa tgc tcc ctc aac ctg cag ctg gtg ggt      624
Ile Ser Gly Asp Ala Val Glu Cys Ser Leu Asn Leu Gln Leu Val Gly
        195                 200                 205

gag gcc tgc ttc acc aat ccg ctg atc gtc gca gtg acc gaa tgg gct      672
Glu Ala Cys Phe Thr Asn Pro Leu Ile Val Ala Val Thr Glu Trp Ala
    210                 215                 220

gcc gcc aac ggc gat gaa atc acc ccg acg gtg ttc ctg tcg atc gag      720
Ala Ala Asn Gly Asp Glu Ile Thr Pro Thr Val Phe Leu Ser Ile Glu
225                 230                 235                 240

acc gac gaa ctg cgc cac atg gcc aac ggt tac cag acc gtc gtt tcc      768
Thr Asp Glu Leu Arg His Met Ala Asn Gly Tyr Gln Thr Val Val Ser
                245                 250                 255

atc gcc aac gat ccg gct tcc gcc aag tat ctc aac acg gac ctg aac      816
Ile Ala Asn Asp Pro Ala Ser Ala Lys Tyr Leu Asn Thr Asp Leu Asn
            260                 265                 270

aac gcc ttc tgg acc cag cag aag tac ttc acg ccg gtg ttg ggc atg      864
Asn Ala Phe Trp Thr Gln Gln Lys Tyr Phe Thr Pro Val Leu Gly Met
        275                 280                 285

ctg ttc gag tat ggc tcc aag ttc aag gtc gag ccg tgg gtc aag acg      912
Leu Phe Glu Tyr Gly Ser Lys Phe Lys Val Glu Pro Trp Val Lys Thr
    290                 295                 300

tgg gac cgc tgg gtg tac gag gac tgg ggc ggc atc tgg atc ggc cgt      960
Trp Asp Arg Trp Val Tyr Glu Asp Trp Gly Gly Ile Trp Ile Gly Arg
305                 310                 315                 320

ctg ggc aag tac ggg gtg gag tcg ccg cgc agc ctc aag gac gcc aag     1008
Leu Gly Lys Tyr Gly Val Glu Ser Pro Arg Ser Leu Lys Asp Ala Lys
                325                 330                 335

cag gac gct tac tgg gct cac cac gac ctg tat ctg ctg gct tat gcg     1056
Gln Asp Ala Tyr Trp Ala His His Asp Leu Tyr Leu Leu Ala Tyr Ala
            340                 345                 350

ctg tgg ccg acc ggc ttc ttc cgt ctg gcg ctg ccg gat cag gaa gaa     1104
```

```
Leu Trp Pro Thr Gly Phe Phe Arg Leu Ala Leu Pro Asp Gln Glu Glu
        355                 360                 365

atg gag tgg ttc gag gcc aac tac ccc ggc tgg tac gac cac tac ggc      1152
Met Glu Trp Phe Glu Ala Asn Tyr Pro Gly Trp Tyr Asp His Tyr Gly
    370                 375                 380

aag atc tac gag gaa tgg cgc gcc cgc ggt tgc gag gat ccg tcc tcg      1200
Lys Ile Tyr Glu Glu Trp Arg Ala Arg Gly Cys Glu Asp Pro Ser Ser
385                 390                 395                 400

ggc ttc atc ccg ctg atg tgg ttc atc gaa aac aac cat ccc atc tac      1248
Gly Phe Ile Pro Leu Met Trp Phe Ile Glu Asn Asn His Pro Ile Tyr
                405                 410                 415

atc gat cgc gtg tcg caa gtg ccg ttc tgc ccg agc ttg gcc aag ggc      1296
Ile Asp Arg Val Ser Gln Val Pro Phe Cys Pro Ser Leu Ala Lys Gly
            420                 425                 430

gcc agc acc ctg cgc gtg cac gag tac aac ggc gag atg cac acc ttc      1344
Ala Ser Thr Leu Arg Val His Glu Tyr Asn Gly Glu Met His Thr Phe
        435                 440                 445

agc gac cag tgg ggc gag cgc atg tgg ctg gcc gag ccg gag cgc tac      1392
Ser Asp Gln Trp Gly Glu Arg Met Trp Leu Ala Glu Pro Glu Arg Tyr
    450                 455                 460

gag tgc cag aac atc ttc gaa cag tac gaa gga cgc gaa ctg tcg gaa      1440
Glu Cys Gln Asn Ile Phe Glu Gln Tyr Glu Gly Arg Glu Leu Ser Glu
465                 470                 475                 480

gtg atc gcc gaa ctg cac ggg ctg cgc agt gat ggc aag acc ctg atc      1488
Val Ile Ala Glu Leu His Gly Leu Arg Ser Asp Gly Lys Thr Leu Ile
                485                 490                 495

gcc cag ccg cat gtc cgt ggc gac aag ctg tgg acg ttg gac gat atc      1536
Ala Gln Pro His Val Arg Gly Asp Lys Leu Trp Thr Leu Asp Asp Ile
            500                 505                 510

aaa cgc ctg aac tgc gtc ttc aag aac ccg gtg aag gca ttc aat tga      1584
Lys Arg Leu Asn Cys Val Phe Lys Asn Pro Val Lys Ala Phe Asn
        515                 520                 525
```

<210> 20
<211> 527
<212> PRT
<213> Methylococcus capsulatas

<400> 20

```
Met Ala Leu Ser Thr Ala Thr Lys Ala Ala Thr Asp Ala Leu Ala Ala
1               5                  10                  15

Asn Arg Ala Pro Thr Ser Val Asn Ala Gln Glu Val His Arg Trp Leu
            20                  25                  30

Gln Ser Phe Asn Trp Asp Phe Lys Asn Asn Arg Thr Lys Tyr Ala Thr
        35                  40                  45

Lys Tyr Lys Met Ala Asn Glu Thr Lys Glu Gln Phe Lys Leu Ile Ala
    50                  55                  60

Lys Glu Tyr Ala Arg Met Glu Ala Val Lys Asp Glu Arg Gln Phe Gly
65                  70                  75                  80

Ser Leu Gln Asp Ala Leu Thr Arg Leu Asn Ala Gly Val Arg Val His
                85                  90                  95

Pro Lys Trp Asn Glu Thr Met Lys Val Val Ser Asn Phe Leu Glu Val
            100                 105                 110

Gly Glu Tyr Asn Ala Ile Ala Ala Thr Gly Met Leu Trp Asp Ser Ala
        115                 120                 125

Gln Ala Ala Glu Gln Lys Asn Gly Tyr Leu Ala Gln Val Leu Asp Glu
```

```
    130                 135                 140

Ile Arg His Thr His Gln Cys Ala Tyr Val Asn Tyr Tyr Phe Ala Lys
145                 150                 155                 160

Asn Gly Gln Asp Pro Ala Gly His Asn Asp Ala Arg Arg Thr Arg Thr
                165                 170                 175

Ile Gly Pro Leu Trp Lys Gly Met Lys Arg Val Phe Ser Asp Gly Phe
            180                 185                 190

Ile Ser Gly Asp Ala Val Glu Cys Ser Leu Asn Leu Gln Leu Val Gly
        195                 200                 205

Glu Ala Cys Phe Thr Asn Pro Leu Ile Val Ala Val Thr Glu Trp Ala
    210                 215                 220

Ala Ala Asn Gly Asp Glu Ile Thr Pro Thr Val Phe Leu Ser Ile Glu
225                 230                 235                 240

Thr Asp Glu Leu Arg His Met Ala Asn Gly Tyr Gln Thr Val Val Ser
                245                 250                 255

Ile Ala Asn Asp Pro Ala Ser Ala Lys Tyr Leu Asn Thr Asp Leu Asn
            260                 265                 270

Asn Ala Phe Trp Thr Gln Gln Lys Tyr Phe Thr Pro Val Leu Gly Met
        275                 280                 285

Leu Phe Glu Tyr Gly Ser Lys Phe Lys Val Glu Pro Trp Val Lys Thr
    290                 295                 300

Trp Asp Arg Trp Val Tyr Glu Asp Trp Gly Gly Ile Trp Ile Gly Arg
305                 310                 315                 320

Leu Gly Lys Tyr Gly Val Glu Ser Pro Arg Ser Leu Lys Asp Ala Lys
                325                 330                 335

Gln Asp Ala Tyr Trp Ala His His Asp Leu Tyr Leu Leu Ala Tyr Ala
            340                 345                 350

Leu Trp Pro Thr Gly Phe Phe Arg Leu Ala Leu Pro Asp Gln Glu Glu
        355                 360                 365

Met Glu Trp Phe Glu Ala Asn Tyr Pro Gly Trp Tyr Asp His Tyr Gly
    370                 375                 380

Lys Ile Tyr Glu Glu Trp Arg Ala Arg Gly Cys Glu Asp Pro Ser Ser
385                 390                 395                 400

Gly Phe Ile Pro Leu Met Trp Phe Ile Glu Asn Asn His Pro Ile Tyr
                405                 410                 415

Ile Asp Arg Val Ser Gln Val Pro Phe Cys Pro Ser Leu Ala Lys Gly
            420                 425                 430

Ala Ser Thr Leu Arg Val His Glu Tyr Asn Gly Glu Met His Thr Phe
        435                 440                 445

Ser Asp Gln Trp Gly Glu Arg Met Trp Leu Ala Glu Pro Glu Arg Tyr
    450                 455                 460

Glu Cys Gln Asn Ile Phe Glu Gln Tyr Glu Gly Arg Glu Leu Ser Glu
465                 470                 475                 480

Val Ile Ala Glu Leu His Gly Leu Arg Ser Asp Gly Lys Thr Leu Ile
                485                 490                 495

Ala Gln Pro His Val Arg Gly Asp Lys Leu Trp Thr Leu Asp Asp Ile
            500                 505                 510

Lys Arg Leu Asn Cys Val Phe Lys Asn Pro Val Lys Ala Phe Asn
        515                 520                 525
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<210> 21

<211> 1170
<212> DNA
<213> Methylococcus capsulatas

<220>
<221> CDS
<222> (1)..(1170)

<400> 21

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atg agc atg tta gga gaa aga cgc cgc ggt ctg acc gat ccg gaa atg        48
Met Ser Met Leu Gly Glu Arg Arg Arg Gly Leu Thr Asp Pro Glu Met
1               5                   10                  15

gcg gcc gtc att ttg aag gcg ctt cct gaa gct ccg ctg gac ggc aac        96
Ala Ala Val Ile Leu Lys Ala Leu Pro Glu Ala Pro Leu Asp Gly Asn
            20                  25                  30

aac aag atg ggt tat ttc gtc acc ccc cgc tgg aaa cgc ttg acg gaa       144
Asn Lys Met Gly Tyr Phe Val Thr Pro Arg Trp Lys Arg Leu Thr Glu
        35                  40                  45

tat gaa gcc ctg acc gtt tat gcg cag ccc aac gcc gac tgg atc gcc       192
Tyr Glu Ala Leu Thr Val Tyr Ala Gln Pro Asn Ala Asp Trp Ile Ala
    50                  55                  60

ggc ggc ctg gac tgg ggc gac tgg acc cag aaa ttc cac ggc ggc cgc       240
Gly Gly Leu Asp Trp Gly Asp Trp Thr Gln Lys Phe His Gly Gly Arg
65                  70                  75                  80

cct tcc tgg ggc aac gag acc acg gag ctg cgc acc gtc gac tgg ttc       288
Pro Ser Trp Gly Asn Glu Thr Thr Glu Leu Arg Thr Val Asp Trp Phe
                85                  90                  95

aag cac cgt gac ccg ctc cgc cgt tgg cat gcg ccg tac gtc aag gac       336
Lys His Arg Asp Pro Leu Arg Arg Trp His Ala Pro Tyr Val Lys Asp
            100                 105                 110

aag gcc gag gaa tgg cgc tac acc gac cgc ttc ctg cag ggt tac tcc       384
Lys Ala Glu Glu Trp Arg Tyr Thr Asp Arg Phe Leu Gln Gly Tyr Ser
        115                 120                 125

gcc gac ggt cag atc cgg gcg atg aac ccg acc tgg cgg gac gag ttc       432
Ala Asp Gly Gln Ile Arg Ala Met Asn Pro Thr Trp Arg Asp Glu Phe
    130                 135                 140

atc aac cgg tat tgg ggc gcc ttc ctg ttc aac gaa tac gga ttg ttc       480
Ile Asn Arg Tyr Trp Gly Ala Phe Leu Phe Asn Glu Tyr Gly Leu Phe
145                 150                 155                 160

aac gct cat tcg cag ggc gcc cgg gag gcg ctg tcg gac gta acc cgc       528
Asn Ala His Ser Gln Gly Ala Arg Glu Ala Leu Ser Asp Val Thr Arg
                165                 170                 175

gtc agc ctg gct ttc tgg ggc ttc gac aag atc gac atc gcc cag atg       576
Val Ser Leu Ala Phe Trp Gly Phe Asp Lys Ile Asp Ile Ala Gln Met
            180                 185                 190

atc caa ctc gaa cgg ggt ttc ctc gcc aag atc gta ccc ggt ttc gac       624
Ile Gln Leu Glu Arg Gly Phe Leu Ala Lys Ile Val Pro Gly Phe Asp
        195                 200                 205

gag tcc aca gcg gtg ccg aag gcc gaa tgg acg aac ggg gag gtc tac       672
Glu Ser Thr Ala Val Pro Lys Ala Glu Trp Thr Asn Gly Glu Val Tyr
    210                 215                 220

aag agc gcc cgt ctg gcc gtg gaa ggg ctg tgg cag gag gtg ttc gac       720
Lys Ser Ala Arg Leu Ala Val Glu Gly Leu Trp Gln Glu Val Phe Asp
225                 230                 235                 240

tgg aac gag agc gct ttc tcg gtg cac gcc gtc tat gac gcg ctg ttc       768
Trp Asn Glu Ser Ala Phe Ser Val His Ala Val Tyr Asp Ala Leu Phe
                245                 250                 255

ggt cag ttc gtc cgc cgc gag ttc ttt cag cgg ctg gct ccc cgc ttc       816
Gly Gln Phe Val Arg Arg Glu Phe Phe Gln Arg Leu Ala Pro Arg Phe
```

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                260                 265                 270

ggc gac aat ctg acg cca ttc ttc atc aac cag gcc cag aca tac ttc      864
Gly Asp Asn Leu Thr Pro Phe Phe Ile Asn Gln Ala Gln Thr Tyr Phe
        275                 280                 285

cag atc gcc aag cag ggc gta cag gat ctg tat tac aac tgt ctg ggt      912
Gln Ile Ala Lys Gln Gly Val Gln Asp Leu Tyr Tyr Asn Cys Leu Gly
    290                 295                 300

gac gat ccg gag ttc agc gat tac aac cgt acc gtg atg cgc aac tgg      960
Asp Asp Pro Glu Phe Ser Asp Tyr Asn Arg Thr Val Met Arg Asn Trp
305                 310                 315                 320

acc ggc aag tgg ctg gag ccc acg atc gcc gct ctg cgc gac ttc atg     1008
Thr Gly Lys Trp Leu Glu Pro Thr Ile Ala Ala Leu Arg Asp Phe Met
                325                 330                 335

ggg ctg ttt gcg aag ctg ccg gcg ggc acc act gac aag gaa gaa atc     1056
Gly Leu Phe Ala Lys Leu Pro Ala Gly Thr Thr Asp Lys Glu Glu Ile
            340                 345                 350

acc gcg tcc ctg tac cgg gtg gtc gac gac tgg atc gag gac tac gcc     1104
Thr Ala Ser Leu Tyr Arg Val Val Asp Asp Trp Ile Glu Asp Tyr Ala
        355                 360                 365

agc gcg atc gac ttc aag gcg gac cgc gat cag atc gtt aaa gcg gtt     1152
Ser Ala Ile Asp Phe Lys Ala Asp Arg Asp Gln Ile Val Lys Ala Val
    370                 375                 380

ctg gca gga ttg aaa taa                                           1170
Leu Ala Gly Leu Lys
385
```

<210> 22
<211> 389
<212> PRT
<213> Methylococcus capsulatas

<400> 22

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Met Ser Met Leu Gly Glu Arg Arg Arg Gly Leu Thr Asp Pro Glu Met
1               5                   10                  15

Ala Ala Val Ile Leu Lys Ala Leu Pro Glu Ala Pro Leu Asp Gly Asn
            20                  25                  30

Asn Lys Met Gly Tyr Phe Val Thr Pro Arg Trp Lys Arg Leu Thr Glu
        35                  40                  45

Tyr Glu Ala Leu Thr Val Tyr Ala Gln Pro Asn Ala Asp Trp Ile Ala
    50                  55                  60

Gly Gly Leu Asp Trp Gly Asp Trp Thr Gln Lys Phe His Gly Gly Arg
65                  70                  75                  80

Pro Ser Trp Gly Asn Glu Thr Thr Glu Leu Arg Thr Val Asp Trp Phe
                85                  90                  95

Lys His Arg Asp Pro Leu Arg Arg Trp His Ala Pro Tyr Val Lys Asp
            100                 105                 110

Lys Ala Glu Glu Trp Arg Tyr Thr Asp Arg Phe Leu Gln Gly Tyr Ser
        115                 120                 125

Ala Asp Gly Gln Ile Arg Ala Met Asn Pro Thr Trp Arg Asp Glu Phe
    130                 135                 140

Ile Asn Arg Tyr Trp Gly Ala Phe Leu Phe Asn Glu Tyr Gly Leu Phe
145                 150                 155                 160

Asn Ala His Ser Gln Gly Ala Arg Glu Ala Leu Ser Asp Val Thr Arg
                165                 170                 175

Val Ser Leu Ala Phe Trp Gly Phe Asp Lys Ile Asp Ile Ala Gln Met
```

180 185 190

Ile Gln Leu Glu Arg Gly Phe Leu Ala Lys Ile Val Pro Gly Phe Asp
195 200 205

Glu Ser Thr Ala Val Pro Lys Ala Glu Trp Thr Asn Gly Glu Val Tyr
210 215 220

Lys Ser Ala Arg Leu Ala Val Glu Gly Leu Trp Gln Glu Val Phe Asp
225 230 235 240

Trp Asn Glu Ser Ala Phe Ser Val His Ala Val Tyr Asp Ala Leu Phe
245 250 255

Gly Gln Phe Val Arg Arg Glu Phe Phe Gln Arg Leu Ala Pro Arg Phe
260 265 270

Gly Asp Asn Leu Thr Pro Phe Phe Ile Asn Gln Ala Gln Thr Tyr Phe
275 280 285

Gln Ile Ala Lys Gln Gly Val Gln Asp Leu Tyr Tyr Asn Cys Leu Gly
290 295 300

Asp Asp Pro Glu Phe Ser Asp Tyr Asn Arg Thr Val Met Arg Asn Trp
305 310 315 320

Thr Gly Lys Trp Leu Glu Pro Thr Ile Ala Ala Leu Arg Asp Phe Met
325 330 335

Gly Leu Phe Ala Lys Leu Pro Ala Gly Thr Thr Asp Lys Glu Glu Ile
340 345 350

Thr Ala Ser Leu Tyr Arg Val Val Asp Asp Trp Ile Glu Asp Tyr Ala
355 360 365

Ser Ala Ile Asp Phe Lys Ala Asp Arg Asp Gln Ile Val Lys Ala Val
370 375 380

Leu Ala Gly Leu Lys
385

<210> 23
<211> 513
<212> DNA
<213> Methylococcus capsulatas

<220>
<221> CDS
<222> (1)..(513)

<400> 23
atg gcg aaa ctg ggt ata cac agc aac gac acc cgc gac gcc tgg gtg 48
Met Ala Lys Leu Gly Ile His Ser Asn Asp Thr Arg Asp Ala Trp Val
1 5 10 15

aac aag atc gcg cag ctc aac acc ctg gaa aaa gcg gcc gag atg ctg 96
Asn Lys Ile Ala Gln Leu Asn Thr Leu Glu Lys Ala Ala Glu Met Leu
20 25 30

aag cag ttc cgg atg gac cac acc acg ccg ttc cgc aac agc tac gaa 144
Lys Gln Phe Arg Met Asp His Thr Thr Pro Phe Arg Asn Ser Tyr Glu
35 40 45

ctg gac aac gac tac ctc tgg atc gag gcc aag ctc gaa gag aag gtc 192
Leu Asp Asn Asp Tyr Leu Trp Ile Glu Ala Lys Leu Glu Glu Lys Val
50 55 60

gcc gtc ctc aag gca cgc gcc ttc aac gag gtg gac ttc cgt cat aag 240
Ala Val Leu Lys Ala Arg Ala Phe Asn Glu Val Asp Phe Arg His Lys
65 70 75 80

acc gct ttc ggc gag gat gcc aag tcc gtt ctg gac ggc acc gtc gcg 288
Thr Ala Phe Gly Glu Asp Ala Lys Ser Val Leu Asp Gly Thr Val Ala
85 90 95

```
aag atg aac gcg gcc aag gac aag tgg gag gcg gag aag atc cat atc      336
Lys Met Asn Ala Ala Lys Asp Lys Trp Glu Ala Glu Lys Ile His Ile
            100                 105                 110

ggt ttc cgc cag gcc tac aag ccg ccg atc atg ccg gtg aac tat ttc      384
Gly Phe Arg Gln Ala Tyr Lys Pro Pro Ile Met Pro Val Asn Tyr Phe
        115                 120                 125

ctg gac ggc gag cgt cag ttg ggg acc cgg ctg atg gaa ctg cgc aac      432
Leu Asp Gly Glu Arg Gln Leu Gly Thr Arg Leu Met Glu Leu Arg Asn
    130                 135                 140

ctc aac tac tac gac acg ccg ctg gaa gaa ctg cgc aaa cag cgc ggt      480
Leu Asn Tyr Tyr Asp Thr Pro Leu Glu Glu Leu Arg Lys Gln Arg Gly
145                 150                 155                 160

gtg cgg gtg gtg cat ctg cag tcg ccg cac tga                          513
Val Arg Val Val His Leu Gln Ser Pro His
                165                 170
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<210> 24
<211> 170
<212> PRT
<213> Methylococcus capsulatas

<400> 24

Met Ala Lys Leu Gly Ile His Ser Asn Asp Thr Arg Asp Ala Trp Val
1   5   10   15

Asn Lys Ile Ala Gln Leu Asn Thr Leu Glu Lys Ala Ala Glu Met Leu
            20   25   30

Lys Gln Phe Arg Met Asp His Thr Thr Pro Phe Arg Asn Ser Tyr Glu
        35   40   45

Leu Asp Asn Asp Tyr Leu Trp Ile Glu Ala Lys Leu Glu Glu Lys Val
    50   55   60

Ala Val Leu Lys Ala Arg Ala Phe Asn Glu Val Asp Phe Arg His Lys
65   70   75   80

Thr Ala Phe Gly Glu Asp Ala Lys Ser Val Leu Asp Gly Thr Val Ala
                85   90   95

Lys Met Asn Ala Ala Lys Asp Lys Trp Glu Ala Glu Lys Ile His Ile
            100   105   110

Gly Phe Arg Gln Ala Tyr Lys Pro Pro Ile Met Pro Val Asn Tyr Phe
        115   120   125

Leu Asp Gly Glu Arg Gln Leu Gly Thr Arg Leu Met Glu Leu Arg Asn
    130   135   140

Leu Asn Tyr Tyr Asp Thr Pro Leu Glu Glu Leu Arg Lys Gln Arg Gly
145   150   155   160

Val Arg Val Val His Leu Gln Ser Pro His
                165   170

<210> 25
<211> 1206
<212> DNA
<213> Pseudomonas oleovorans

<220>
<221> CDS
<222> (1)..(1206)

<400> 25
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atg ctt gag aaa cac aga gtt ctg gat tcc gct cca gag tac gta gat       48
Met Leu Glu Lys His Arg Val Leu Asp Ser Ala Pro Glu Tyr Val Asp
```

```
1               5                  10                  15

aaa aag aaa tat ctc tgg ata cta tca act ttg tgg ccg gct act ccg      96
Lys Lys Lys Tyr Leu Trp Ile Leu Ser Thr Leu Trp Pro Ala Thr Pro
            20                  25                  30

atg atc gga atc tgg ctt gca aat gaa act ggt tgg ggg att ttt tat     144
Met Ile Gly Ile Trp Leu Ala Asn Glu Thr Gly Trp Gly Ile Phe Tyr
        35                  40                  45

ggg ctg gta ttg ctc gta tgg tac ggc gca ctt cca ttg ctt gat gcg     192
Gly Leu Val Leu Leu Val Trp Tyr Gly Ala Leu Pro Leu Leu Asp Ala
    50                  55                  60

atg ttt ggt gag gac ttt aat aat ccg cct gaa gaa gtg gtg ccg aaa     240
Met Phe Gly Glu Asp Phe Asn Asn Pro Pro Glu Glu Val Val Pro Lys
65                  70                  75                  80

cta gag aag gag cgg tac tat cga gtt ttg aca tat cta aca gtt cct     288
Leu Glu Lys Glu Arg Tyr Tyr Arg Val Leu Thr Tyr Leu Thr Val Pro
                85                  90                  95

atg cat tac gct gca tta att gtg tca gca tgg tgg gtc gga act cag     336
Met His Tyr Ala Ala Leu Ile Val Ser Ala Trp Trp Val Gly Thr Gln
            100                 105                 110

cca atg tct tgg ctt gaa att ggt gcg ctt gcc ttg tca ctg ggt atc     384
Pro Met Ser Trp Leu Glu Ile Gly Ala Leu Ala Leu Ser Leu Gly Ile
        115                 120                 125

gtg aac gga cta gcg ctc aat aca gga cac gaa ctc ggt cac aag aag     432
Val Asn Gly Leu Ala Leu Asn Thr Gly His Glu Leu Gly His Lys Lys
    130                 135                 140

gag act ttt gat cgt tgg atg gcc aaa att gtg ttg gct gtc gta ggg     480
Glu Thr Phe Asp Arg Trp Met Ala Lys Ile Val Leu Ala Val Val Gly
145                 150                 155                 160

tac ggt cac ttc ttt att gag cat aat aag ggt cat cac cgt gat gtc     528
Tyr Gly His Phe Phe Ile Glu His Asn Lys Gly His His Arg Asp Val
                165                 170                 175

gct aca ccg atg gat cct gca aca tcc cgg atg gga gaa agc att tat     576
Ala Thr Pro Met Asp Pro Ala Thr Ser Arg Met Gly Glu Ser Ile Tyr
            180                 185                 190

aag ttt tca atc cgt gag atc cca gga gca ttt att cgt gct tgg ggg     624
Lys Phe Ser Ile Arg Glu Ile Pro Gly Ala Phe Ile Arg Ala Trp Gly
        195                 200                 205

ctt gag gaa caa cgc ctt tcg cgc cgt ggc caa agc gtt tgg agt ttc     672
Leu Glu Glu Gln Arg Leu Ser Arg Arg Gly Gln Ser Val Trp Ser Phe
    210                 215                 220

gat aat gaa atc ctc caa cca atg atc atc aca gtt att ctt tac gcc     720
Asp Asn Glu Ile Leu Gln Pro Met Ile Ile Thr Val Ile Leu Tyr Ala
225                 230                 235                 240

gtt ctc ctt gcc ttg ttt gga cct aag atg ctg gtg ttc ctg ccg att     768
Val Leu Leu Ala Leu Phe Gly Pro Lys Met Leu Val Phe Leu Pro Ile
                245                 250                 255

caa atg gct ttc ggt tgg tgg cag ctg acc agt gcg aac tat att gaa     816
Gln Met Ala Phe Gly Trp Trp Gln Leu Thr Ser Ala Asn Tyr Ile Glu
            260                 265                 270

cat tac ggc ttg ctc cgt caa aaa atg gag gac ggt cga tat gag cat     864
His Tyr Gly Leu Leu Arg Gln Lys Met Glu Asp Gly Arg Tyr Glu His
        275                 280                 285

caa aag ccg cac cat tct tgg aat agt aat cac atc gtc tct aat cta     912
Gln Lys Pro His His Ser Trp Asn Ser Asn His Ile Val Ser Asn Leu
    290                 295                 300

gtg ctg ttc cac ctt cag cgg cac tcg gat cac cac gcg cat cca aca     960
Val Leu Phe His Leu Gln Arg His Ser Asp His His Ala His Pro Thr
```

```
305                 310                 315                 320

cgt tct tat cag tca ctt cgg gat ttt ccc ggc ctg ccg gct ctt ccg      1008
Arg Ser Tyr Gln Ser Leu Arg Asp Phe Pro Gly Leu Pro Ala Leu Pro
                325                 330                 335

acg ggt tac cct ggt gca ttt ttg atg gcg atg att cct cag tgg ttt      1056
Thr Gly Tyr Pro Gly Ala Phe Leu Met Ala Met Ile Pro Gln Trp Phe
            340                 345                 350

aga tca gtt atg gat ccc aag gta gta gat tgg gct ggt ggt gac ctt      1104
Arg Ser Val Met Asp Pro Lys Val Val Asp Trp Ala Gly Gly Asp Leu
        355                 360                 365

aat aag atc caa att gat gat tcg atg cga gaa acc tat ttg aaa aaa      1152
Asn Lys Ile Gln Ile Asp Asp Ser Met Arg Glu Thr Tyr Leu Lys Lys
    370                 375                 380

ttt ggc act agt agt gct ggt cat agt tcg agt acc tct gcg gta gca      1200
Phe Gly Thr Ser Ser Ala Gly His Ser Ser Ser Thr Ser Ala Val Ala
385                 390                 395                 400

tcg tag                                                             1206
Ser
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<210> 26
<211> 401
<212> PRT
<213> Pseudomonas oleovorans

<400> 26

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Met Leu Glu Lys His Arg Val Leu Asp Ser Ala Pro Glu Tyr Val Asp
1               5                   10                  15

Lys Lys Lys Tyr Leu Trp Ile Leu Ser Thr Leu Trp Pro Ala Thr Pro
            20                  25                  30

Met Ile Gly Ile Trp Leu Ala Asn Glu Thr Gly Trp Gly Ile Phe Tyr
        35                  40                  45

Gly Leu Val Leu Leu Val Trp Tyr Gly Ala Leu Pro Leu Leu Asp Ala
    50                  55                  60

Met Phe Gly Glu Asp Phe Asn Asn Pro Pro Glu Glu Val Val Pro Lys
65                  70                  75                  80

Leu Glu Lys Glu Arg Tyr Tyr Arg Val Leu Thr Tyr Leu Thr Val Pro
                85                  90                  95

Met His Tyr Ala Ala Leu Ile Val Ser Ala Trp Trp Val Gly Thr Gln
            100                 105                 110

Pro Met Ser Trp Leu Glu Ile Gly Ala Leu Ala Leu Ser Leu Gly Ile
        115                 120                 125

Val Asn Gly Leu Ala Leu Asn Thr Gly His Glu Leu Gly His Lys Lys
    130                 135                 140

Glu Thr Phe Asp Arg Trp Met Ala Lys Ile Val Leu Ala Val Val Gly
145                 150                 155                 160

Tyr Gly His Phe Phe Ile Glu His Asn Lys Gly His His Arg Asp Val
                165                 170                 175

Ala Thr Pro Met Asp Pro Ala Thr Ser Arg Met Gly Glu Ser Ile Tyr
            180                 185                 190

Lys Phe Ser Ile Arg Glu Ile Pro Gly Ala Phe Ile Arg Ala Trp Gly
        195                 200                 205

Leu Glu Glu Gln Arg Leu Ser Arg Arg Gly Gln Ser Val Trp Ser Phe
    210                 215                 220
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Asp Asn Glu Ile Leu Gln Pro Met Ile Ile Thr Val Ile Leu Tyr Ala
225 230 235 240

Val Leu Leu Ala Leu Phe Gly Pro Lys Met Leu Val Phe Leu Pro Ile
245 250 255

Gln Met Ala Phe Gly Trp Trp Gln Leu Thr Ser Ala Asn Tyr Ile Glu
260 265 270

His Tyr Gly Leu Leu Arg Gln Lys Met Glu Asp Gly Arg Tyr Glu His
275 280 285

Gln Lys Pro His His Ser Trp Asn Ser Asn His Ile Val Ser Asn Leu
290 295 300

Val Leu Phe His Leu Gln Arg His Ser Asp His His Ala His Pro Thr
305 310 315 320

Arg Ser Tyr Gln Ser Leu Arg Asp Phe Pro Gly Leu Pro Ala Leu Pro
325 330 335

Thr Gly Tyr Pro Gly Ala Phe Leu Met Ala Met Ile Pro Gln Trp Phe
340 345 350

Arg Ser Val Met Asp Pro Lys Val Val Asp Trp Ala Gly Gly Asp Leu
355 360 365

Asn Lys Ile Gln Ile Asp Asp Ser Met Arg Glu Thr Tyr Leu Lys Lys
370 375 380

Phe Gly Thr Ser Ser Ala Gly His Ser Ser Ser Thr Ser Ala Val Ala
385 390 395 400

Ser

<210> 27
<211> 1560
<212> DNA
<213> Burkholderia cepacia

<220>
<221> CDS
<222> (1)..(1560)

<400> 27
atg gac act tct gtg cag aag aag aaa ctc ggt tta aag aat cgc tac 48
Met Asp Thr Ser Val Gln Lys Lys Lys Leu Gly Leu Lys Asn Arg Tyr
1 5 10 15

gca gcg atg acc cgc ggt ctt ggc tgg cag acc agc tac cag ccg atg 96
Ala Ala Met Thr Arg Gly Leu Gly Trp Gln Thr Ser Tyr Gln Pro Met
20 25 30

gag aaa gtg ttt ccg tac gac aag tac gaa ggc atc aag atc cac gat 144
Glu Lys Val Phe Pro Tyr Asp Lys Tyr Glu Gly Ile Lys Ile His Asp
35 40 45

tgg gat aaa tgg gaa gac ccc ttc cgc ctg acc atg gac gcc tac tgg 192
Trp Asp Lys Trp Glu Asp Pro Phe Arg Leu Thr Met Asp Ala Tyr Trp
50 55 60

aaa tat cag ggc gag aag gaa aaa aag ctt tac gcc gtc atc gac gct 240
Lys Tyr Gln Gly Glu Lys Glu Lys Lys Leu Tyr Ala Val Ile Asp Ala
65 70 75 80

ttc gcg cag aac aac ggg cag ttg agc att tcc gac gcg cga tat gtc 288
Phe Ala Gln Asn Asn Gly Gln Leu Ser Ile Ser Asp Ala Arg Tyr Val
85 90 95

aac gca ctc aag gtg ttt atc cag ggt gtg aca ccg ttg gag tat atg 336
Asn Ala Leu Lys Val Phe Ile Gln Gly Val Thr Pro Leu Glu Tyr Met
100 105 110

```
gca cac cga ggt ttt gcc cac att ggt cgg cat ttt acg ggt gaa ggg      384
Ala His Arg Gly Phe Ala His Ile Gly Arg His Phe Thr Gly Glu Gly
        115                 120                 125

gca cgt gtt gct tgc cag atg cag tcc atc gac gag ctg cgt cac ttc      432
Ala Arg Val Ala Cys Gln Met Gln Ser Ile Asp Glu Leu Arg His Phe
    130                 135                 140

cag acc gaa atg cat gct ctc tcg cac tac aac aag tat ttt aac ggt      480
Gln Thr Glu Met His Ala Leu Ser His Tyr Asn Lys Tyr Phe Asn Gly
145                 150                 155                 160

ctg cac aac tcc atc cat tgg tac gac cgg gtt tgg tat ttg tcg gtg      528
Leu His Asn Ser Ile His Trp Tyr Asp Arg Val Trp Tyr Leu Ser Val
                165                 170                 175

ccc aag tca ttt ttt gaa gac gcg gcc acc ggt gga ccg ttc gag ttt      576
Pro Lys Ser Phe Phe Glu Asp Ala Ala Thr Gly Gly Pro Phe Glu Phe
            180                 185                 190

ctt acc gcg gtg agc ttt tcg ttc gaa tat gtg ttg acc aac ctg ctg      624
Leu Thr Ala Val Ser Phe Ser Phe Glu Tyr Val Leu Thr Asn Leu Leu
        195                 200                 205

ttt gtc ccc ttc atg tcg ggt gct gct tac aac ggg gac atg tct acg      672
Phe Val Pro Phe Met Ser Gly Ala Ala Tyr Asn Gly Asp Met Ser Thr
    210                 215                 220

gtc act ttc ggt ttt tcg gcg caa agt gac gaa tcg cgc cac atg aca      720
Val Thr Phe Gly Phe Ser Ala Gln Ser Asp Glu Ser Arg His Met Thr
225                 230                 235                 240

ctc ggc atc gaa tgc atc aag ttc atg cta gaa cag gat ccg gac aac      768
Leu Gly Ile Glu Cys Ile Lys Phe Met Leu Glu Gln Asp Pro Asp Asn
                245                 250                 255

gtg ccc atc gtg cag cgc tgg atc gac aag tgg ttc tgg cgc ggc tat      816
Val Pro Ile Val Gln Arg Trp Ile Asp Lys Trp Phe Trp Arg Gly Tyr
            260                 265                 270

cgg ctg ttg agc atc gtg gcc atg atg cag gac tac atg ctg ccc aac      864
Arg Leu Leu Ser Ile Val Ala Met Met Gln Asp Tyr Met Leu Pro Asn
        275                 280                 285

cgg gtg atg agc tgg cgc gag agc tgg gag atg tac gtc gag cag aac      912
Arg Val Met Ser Trp Arg Glu Ser Trp Glu Met Tyr Val Glu Gln Asn
    290                 295                 300

ggc ggc gcg ctg ttc aag gat ctt gcg cgt tat ggc atc cgc aag ccc      960
Gly Gly Ala Leu Phe Lys Asp Leu Ala Arg Tyr Gly Ile Arg Lys Pro
305                 310                 315                 320

aag ggc tgg gac cag gct tgc gaa ggc aag gac cac atc agc cat cag     1008
Lys Gly Trp Asp Gln Ala Cys Glu Gly Lys Asp His Ile Ser His Gln
                325                 330                 335

acc ttc gcc gta ttc tat aac tat aac gcc gcg gcc ccc atc cac acc     1056
Thr Phe Ala Val Phe Tyr Asn Tyr Asn Ala Ala Ala Pro Ile His Thr
            340                 345                 350

tgg gtt ccc aca aaa gaa gaa atg gga tgg ctg tcg gag aag tac ccc     1104
Trp Val Pro Thr Lys Glu Glu Met Gly Trp Leu Ser Glu Lys Tyr Pro
        355                 360                 365

gag acg ttc gac aag tat tac cgt ccg cgt tgg gac tac tgg cgc gag     1152
Glu Thr Phe Asp Lys Tyr Tyr Arg Pro Arg Trp Asp Tyr Trp Arg Glu
    370                 375                 380

cag gcc gcc aag ggc aac cgt ttc tac aac aag acg ctg ccg atg ctc     1200
Gln Ala Ala Lys Gly Asn Arg Phe Tyr Asn Lys Thr Leu Pro Met Leu
385                 390                 395                 400

tgc act acc tgc cag att ccg atg ata ttc acc gag cct ggc gac gca     1248
Cys Thr Thr Cys Gln Ile Pro Met Ile Phe Thr Glu Pro Gly Asp Ala
                405                 410                 415
```

```
acc aag atc tgc tat cgc gag tcg gcc tac ctc ggc gac aag tat cac      1296
Thr Lys Ile Cys Tyr Arg Glu Ser Ala Tyr Leu Gly Asp Lys Tyr His
            420                 425                 430

ttc tgc agc gac cac tgc aag gag att ttt gac aac gaa ccc gaa aag      1344
Phe Cys Ser Asp His Cys Lys Glu Ile Phe Asp Asn Glu Pro Glu Lys
        435                 440                 445

ttc gtg cag tca tgg ctt ccg ccg cag caa gtg tat caa gga aac tgt      1392
Phe Val Gln Ser Trp Leu Pro Pro Gln Gln Val Tyr Gln Gly Asn Cys
    450                 455                 460

ttc aag ccg gat gcc gat ccg acc aag gag ggt ttt gat ccc ttg atg      1440
Phe Lys Pro Asp Ala Asp Pro Thr Lys Glu Gly Phe Asp Pro Leu Met
465                 470                 475                 480

gcc ttg ctc gac tac tac aac ctg aat gta ggc cgg gac aac ttc gat      1488
Ala Leu Leu Asp Tyr Tyr Asn Leu Asn Val Gly Arg Asp Asn Phe Asp
                485                 490                 495

ttc gag gga tcg gaa gac caa aag aac ttt gct gcc tgg cgt gga gag      1536
Phe Glu Gly Ser Glu Asp Gln Lys Asn Phe Ala Ala Trp Arg Gly Glu
            500                 505                 510

gtc ttg caa gga gaa gcc aaa tga                                     1560
Val Leu Gln Gly Glu Ala Lys
        515
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<210> 28
<211> 519
<212> PRT
<213> Burkholderia cepacia

<400> 28

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Met Asp Thr Ser Val Gln Lys Lys Lys Leu Gly Leu Lys Asn Arg Tyr
1               5                   10                  15

Ala Ala Met Thr Arg Gly Leu Gly Trp Gln Thr Ser Tyr Gln Pro Met
            20                  25                  30

Glu Lys Val Phe Pro Tyr Asp Lys Tyr Glu Gly Ile Lys Ile His Asp
        35                  40                  45

Trp Asp Lys Trp Glu Asp Pro Phe Arg Leu Thr Met Asp Ala Tyr Trp
    50                  55                  60

Lys Tyr Gln Gly Glu Lys Glu Lys Lys Leu Tyr Ala Val Ile Asp Ala
65                  70                  75                  80

Phe Ala Gln Asn Asn Gly Gln Leu Ser Ile Ser Asp Ala Arg Tyr Val
                85                  90                  95

Asn Ala Leu Lys Val Phe Ile Gln Gly Val Thr Pro Leu Glu Tyr Met
            100                 105                 110

Ala His Arg Gly Phe Ala His Ile Gly Arg His Phe Thr Gly Glu Gly
        115                 120                 125

Ala Arg Val Ala Cys Gln Met Gln Ser Ile Asp Glu Leu Arg His Phe
    130                 135                 140

Gln Thr Glu Met His Ala Leu Ser His Tyr Asn Lys Tyr Phe Asn Gly
145                 150                 155                 160

Leu His Asn Ser Ile His Trp Tyr Asp Arg Val Trp Tyr Leu Ser Val
                165                 170                 175

Pro Lys Ser Phe Phe Glu Asp Ala Ala Thr Gly Gly Pro Phe Glu Phe
            180                 185                 190

Leu Thr Ala Val Ser Phe Ser Phe Glu Tyr Val Leu Thr Asn Leu Leu
        195                 200                 205
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Phe Val Pro Phe Met Ser Gly Ala Ala Tyr Asn Gly Asp Met Ser Thr
210 215 220

Val Thr Phe Gly Phe Ser Ala Gln Ser Asp Glu Ser Arg His Met Thr
225 230 235 240

Leu Gly Ile Glu Cys Ile Lys Phe Met Leu Glu Gln Asp Pro Asp Asn
245 250 255

Val Pro Ile Val Gln Arg Trp Ile Asp Lys Trp Phe Trp Arg Gly Tyr
260 265 270

Arg Leu Leu Ser Ile Val Ala Met Met Gln Asp Tyr Met Leu Pro Asn
275 280 285

Arg Val Met Ser Trp Arg Glu Ser Trp Glu Met Tyr Val Glu Gln Asn
290 295 300

Gly Gly Ala Leu Phe Lys Asp Leu Ala Arg Tyr Gly Ile Arg Lys Pro
305 310 315 320

Lys Gly Trp Asp Gln Ala Cys Glu Gly Lys Asp His Ile Ser His Gln
325 330 335

Thr Phe Ala Val Phe Tyr Asn Tyr Asn Ala Ala Ala Pro Ile His Thr
340 345 350

Trp Val Pro Thr Lys Glu Glu Met Gly Trp Leu Ser Glu Lys Tyr Pro
355 360 365

Glu Thr Phe Asp Lys Tyr Tyr Arg Pro Arg Trp Asp Tyr Trp Arg Glu
370 375 380

Gln Ala Ala Lys Gly Asn Arg Phe Tyr Asn Lys Thr Leu Pro Met Leu
385 390 395 400

Cys Thr Thr Cys Gln Ile Pro Met Ile Phe Thr Glu Pro Gly Asp Ala
405 410 415

Thr Lys Ile Cys Tyr Arg Glu Ser Ala Tyr Leu Gly Asp Lys Tyr His
420 425 430

Phe Cys Ser Asp His Cys Lys Glu Ile Phe Asp Asn Glu Pro Glu Lys
435 440 445

Phe Val Gln Ser Trp Leu Pro Pro Gln Gln Val Tyr Gln Gly Asn Cys
450 455 460

Phe Lys Pro Asp Ala Asp Pro Thr Lys Glu Gly Phe Asp Pro Leu Met
465 470 475 480

Ala Leu Leu Asp Tyr Tyr Asn Leu Asn Val Gly Arg Asp Asn Phe Asp
485 490 495

Phe Glu Gly Ser Glu Asp Gln Lys Asn Phe Ala Ala Trp Arg Gly Glu
500 505 510

Val Leu Gln Gly Glu Ala Lys
515

<210> 29
<211> 996
<212> DNA
<213> Burkholderia cepacia

<220>
<221> CDS
<222> (1)..(996)

<400> 29
atg acc atc gat ttg aag acg cgg gaa atc aaa cca ctg cgt cac acc 48
Met Thr Ile Asp Leu Lys Thr Arg Glu Ile Lys Pro Leu Arg His Thr
1 5 10 15

```
tac acg cac gtg gct caa tac atc ggg gcc gat aaa gcc gct tcg cgc        96
Tyr Thr His Val Ala Gln Tyr Ile Gly Ala Asp Lys Ala Ala Ser Arg
            20                  25                  30

tat cag gaa ggc act gta ggt gct caa ccc gca gcg aat ttt cat tac       144
Tyr Gln Glu Gly Thr Val Gly Ala Gln Pro Ala Ala Asn Phe His Tyr
        35                  40                  45

cgg ccc acg tgg gat ccc gag cat gaa ctg ttc gac acg tcg cgt acc       192
Arg Pro Thr Trp Asp Pro Glu His Glu Leu Phe Asp Thr Ser Arg Thr
    50                  55                  60

gcg att caa atg aag gac tgg tat gcg ctg aaa gac ccg cgt cag ttc       240
Ala Ile Gln Met Lys Asp Trp Tyr Ala Leu Lys Asp Pro Arg Gln Phe
65                  70                  75                  80

tac tac gcg tcg tgg acg atg acc cga gcg cgg cag caa gac gcg atg       288
Tyr Tyr Ala Ser Trp Thr Met Thr Arg Ala Arg Gln Gln Asp Ala Met
                85                  90                  95

gaa tcc aac ttc gag ttt gtc gag tcg cgc ggc atg atc gat ctc gtt       336
Glu Ser Asn Phe Glu Phe Val Glu Ser Arg Gly Met Ile Asp Leu Val
            100                 105                 110

tcc gat gag gtt cga caa cgg gcg ctt tcc gtt ctc gtg cct ttg cgt       384
Ser Asp Glu Val Arg Gln Arg Ala Leu Ser Val Leu Val Pro Leu Arg
        115                 120                 125

cac gcg gcc tgg ggc gcg aac atg aac aac tcc cag atc tgt gcc cta       432
His Ala Ala Trp Gly Ala Asn Met Asn Asn Ser Gln Ile Cys Ala Leu
    130                 135                 140

ggt tat ggc acg acc ttc act gcg ccg gct atg ttc cac gca atg gac       480
Gly Tyr Gly Thr Thr Phe Thr Ala Pro Ala Met Phe His Ala Met Asp
145                 150                 155                 160

aat ctg ggt gta gcg cag tat ctc aca cga ctg gcg ctg gta atg tct       528
Asn Leu Gly Val Ala Gln Tyr Leu Thr Arg Leu Ala Leu Val Met Ser
                165                 170                 175

gga ccc gat ctt ctt gac gaa gcc aag caa gcc tgg atg acg agt ccc       576
Gly Pro Asp Leu Leu Asp Glu Ala Lys Gln Ala Trp Met Thr Ser Pro
            180                 185                 190

gat tgg caa ccg ttg cgt cgt tat gtg gaa aac act ctg gtg ctg caa       624
Asp Trp Gln Pro Leu Arg Arg Tyr Val Glu Asn Thr Leu Val Leu Gln
        195                 200                 205

gat ccg gtg gaa ctg ttc atc gcc caa aat ctg gcg ctc gac ggt ctt       672
Asp Pro Val Glu Leu Phe Ile Ala Gln Asn Leu Ala Leu Asp Gly Leu
    210                 215                 220

ctt tat ccc atg atc tac ggc gct ttc gtc gac gat tac atc gca ctc       720
Leu Tyr Pro Met Ile Tyr Gly Ala Phe Val Asp Asp Tyr Ile Ala Leu
225                 230                 235                 240

aac ggt ggt agc gca gtg gca atg cta acc act ttc atg ccc gag tgg       768
Asn Gly Gly Ser Ala Val Ala Met Leu Thr Thr Phe Met Pro Glu Trp
                245                 250                 255

cat gac gaa tcc agt cgc tgg gtc gat gcg gta gta aag acc atg gcg       816
His Asp Glu Ser Ser Arg Trp Val Asp Ala Val Val Lys Thr Met Ala
            260                 265                 270

acg gaa tcg gag gat aac aaa gcg ctg ctc att cac tgg ttg cgt acc       864
Thr Glu Ser Glu Asp Asn Lys Ala Leu Leu Ile His Trp Leu Arg Thr
        275                 280                 285

tgg gaa gat cag gcg gcg tca gcg ttg ttg cct gtc gct gaa atg gct       912
Trp Glu Asp Gln Ala Ala Ser Ala Leu Leu Pro Val Ala Glu Met Ala
    290                 295                 300

ttg gcg gaa aac ggc cac gac gcc ttg gaa gaa gta agg cag caa ctt       960
Leu Ala Glu Asn Gly His Asp Ala Leu Glu Glu Val Arg Gln Gln Leu
305                 310                 315                 320
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cgt gcc cgc gtt gcg aag gcc ggg att gtt ctg taa 996
Arg Ala Arg Val Ala Lys Ala Gly Ile Val Leu
325 330

<210> 30
<211> 331
<212> PRT
<213> Burkholderia cepacia

<400> 30

Met Thr Ile Asp Leu Lys Thr Arg Glu Ile Lys Pro Leu Arg His Thr
1 5 10 15

Tyr Thr His Val Ala Gln Tyr Ile Gly Ala Asp Lys Ala Ala Ser Arg
20 25 30

Tyr Gln Glu Gly Thr Val Gly Ala Gln Pro Ala Ala Asn Phe His Tyr
35 40 45

Arg Pro Thr Trp Asp Pro Glu His Glu Leu Phe Asp Thr Ser Arg Thr
50 55 60

Ala Ile Gln Met Lys Asp Trp Tyr Ala Leu Lys Asp Pro Arg Gln Phe
65 70 75 80

Tyr Tyr Ala Ser Trp Thr Met Thr Arg Ala Arg Gln Gln Asp Ala Met
85 90 95

Glu Ser Asn Phe Glu Phe Val Glu Ser Arg Gly Met Ile Asp Leu Val
100 105 110

Ser Asp Glu Val Arg Gln Arg Ala Leu Ser Val Leu Val Pro Leu Arg
115 120 125

His Ala Ala Trp Gly Ala Asn Met Asn Asn Ser Gln Ile Cys Ala Leu
130 135 140

Gly Tyr Gly Thr Thr Phe Thr Ala Pro Ala Met Phe His Ala Met Asp
145 150 155 160

Asn Leu Gly Val Ala Gln Tyr Leu Thr Arg Leu Ala Leu Val Met Ser
165 170 175

Gly Pro Asp Leu Leu Asp Glu Ala Lys Gln Ala Trp Met Thr Ser Pro
180 185 190

Asp Trp Gln Pro Leu Arg Arg Tyr Val Glu Asn Thr Leu Val Leu Gln
195 200 205

Asp Pro Val Glu Leu Phe Ile Ala Gln Asn Leu Ala Leu Asp Gly Leu
210 215 220

Leu Tyr Pro Met Ile Tyr Gly Ala Phe Val Asp Asp Tyr Ile Ala Leu
225 230 235 240

Asn Gly Gly Ser Ala Val Ala Met Leu Thr Thr Phe Met Pro Glu Trp
245 250 255

His Asp Glu Ser Ser Arg Trp Val Asp Ala Val Val Lys Thr Met Ala
260 265 270

Thr Glu Ser Glu Asp Asn Lys Ala Leu Leu Ile His Trp Leu Arg Thr
275 280 285

Trp Glu Asp Gln Ala Ala Ser Ala Leu Leu Pro Val Ala Glu Met Ala
290 295 300

Leu Ala Glu Asn Gly His Asp Ala Leu Glu Glu Val Arg Gln Gln Leu
305 310 315 320

Arg Ala Arg Val Ala Lys Ala Gly Ile Val Leu
325 330

<210> 31
<211> 357
<212> DNA
<213> Burkholderia cepacia

<220>
<221> CDS
<222> (1)..(357)

<400> 31
atg agc gtt gtt gcc ctc aaa ccc tac aag ttc ccg gca cga gac gcg 48
Met Ser Val Val Ala Leu Lys Pro Tyr Lys Phe Pro Ala Arg Asp Ala
1 5 10 15

cgc gaa aac ttt ccg gcg ccg ttg ctg ttt atc ggc tgg gaa gac cat 96
Arg Glu Asn Phe Pro Ala Pro Leu Leu Phe Ile Gly Trp Glu Asp His
20 25 30

ctg ttg ttt gcg gca cct gtt gcc ttg ccc ctg ccg tcg gac acg ttg 144
Leu Leu Phe Ala Ala Pro Val Ala Leu Pro Leu Pro Ser Asp Thr Leu
35 40 45

ttc ggt gcg ctg tgc acc cag gtg ttg ccc ggc act tat ggc tat cac 192
Phe Gly Ala Leu Cys Thr Gln Val Leu Pro Gly Thr Tyr Gly Tyr His
50 55 60

ccc gat ttc tca aag atc gac tgg agc cag gtg cag tgg ttt aag tcc 240
Pro Asp Phe Ser Lys Ile Asp Trp Ser Gln Val Gln Trp Phe Lys Ser
65 70 75 80

ggc cag ccg tgg cat ccc gac ccg gcg aag tcg ctg gct gaa aac ggt 288
Gly Gln Pro Trp His Pro Asp Pro Ala Lys Ser Leu Ala Glu Asn Gly
85 90 95

ctg acg cac aaa gac gtg atc cgc ttt cgc acg cct ggc ttg aac ggt 336
Leu Thr His Lys Asp Val Ile Arg Phe Arg Thr Pro Gly Leu Asn Gly
100 105 110

ctg agc ggt tcc tgc aat tga 357
Leu Ser Gly Ser Cys Asn
115

<210> 32
<211> 118
<212> PRT
<213> Burkholderia cepacia

<400> 32

Met Ser Val Val Ala Leu Lys Pro Tyr Lys Phe Pro Ala Arg Asp Ala
1 5 10 15

Arg Glu Asn Phe Pro Ala Pro Leu Leu Phe Ile Gly Trp Glu Asp His
20 25 30

Leu Leu Phe Ala Ala Pro Val Ala Leu Pro Leu Pro Ser Asp Thr Leu
35 40 45

Phe Gly Ala Leu Cys Thr Gln Val Leu Pro Gly Thr Tyr Gly Tyr His
50 55 60

Pro Asp Phe Ser Lys Ile Asp Trp Ser Gln Val Gln Trp Phe Lys Ser
65 70 75 80

Gly Gln Pro Trp His Pro Asp Pro Ala Lys Ser Leu Ala Glu Asn Gly
85 90 95

Leu Thr His Lys Asp Val Ile Arg Phe Arg Thr Pro Gly Leu Asn Gly
100 105 110

Leu Ser Gly Ser Cys Asn
115

<210> 33
<211> 1143
<212> DNA
<213> Bacillus stearothermophilus

<220>
<221> CDS
<222> (1)..(1143)

<400> 33

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atg gaa aaa aat aaa atg tta ata gaa gaa aag ttg gac act gct gct        48
Met Glu Lys Asn Lys Met Leu Ile Glu Glu Lys Leu Asp Thr Ala Ala
1               5                   10                  15

ctt ctt gct aag gcg gag gaa ata ggc cgg att gct gag gaa gag gcg        96
Leu Leu Ala Lys Ala Glu Glu Ile Gly Arg Ile Ala Glu Glu Glu Ala
            20                  25                  30

ggt gaa gcg gac cgc aat gcc tgt ttc tcc gac cgg gtg gct agg gcc       144
Gly Glu Ala Asp Arg Asn Ala Cys Phe Ser Asp Arg Val Ala Arg Ala
        35                  40                  45

att aaa gaa gct gga ttc cac aag ctc atg cgt ccc aag cag tac gga       192
Ile Lys Glu Ala Gly Phe His Lys Leu Met Arg Pro Lys Gln Tyr Gly
    50                  55                  60

gga ctg caa gta gac ttg cga act tac ggg gag att gtc cgc aca gtg       240
Gly Leu Gln Val Asp Leu Arg Thr Tyr Gly Glu Ile Val Arg Thr Val
65                  70                  75                  80

gcc cgg tac agt gtt gcc gca gga tgg ctg acc tat ttt tat tcc atg       288
Ala Arg Tyr Ser Val Ala Ala Gly Trp Leu Thr Tyr Phe Tyr Ser Met
                85                  90                  95

cat gag gtt tgg gct gca tat ctg cct cca aaa ggc aga gaa gaa att       336
His Glu Val Trp Ala Ala Tyr Leu Pro Pro Lys Gly Arg Glu Glu Ile
            100                 105                 110

ttt gga caa gga ggg ctg ttg gca gac gtc gtt gcc cct gtt ggc cgg       384
Phe Gly Gln Gly Gly Leu Leu Ala Asp Val Val Ala Pro Val Gly Arg
        115                 120                 125

gtg gag aag gac ggg gac ggc tac cgt ctc tat ggg cag tgg aac ttc       432
Val Glu Lys Asp Gly Asp Gly Tyr Arg Leu Tyr Gly Gln Trp Asn Phe
    130                 135                 140

tgt agc ggt gtc ctc cat agt gac tgg atc gga ctt ggc gcc atg atg       480
Cys Ser Gly Val Leu His Ser Asp Trp Ile Gly Leu Gly Ala Met Met
145                 150                 155                 160

gag ctg cct gac ggc aat agt cct gag tac tgt ttg tta gtg ctg cct       528
Glu Leu Pro Asp Gly Asn Ser Pro Glu Tyr Cys Leu Leu Val Leu Pro
                165                 170                 175

aag tcg gat gtc cag atc gta gaa aat tgg gat acc atg ggc ctc cgc       576
Lys Ser Asp Val Gln Ile Val Glu Asn Trp Asp Thr Met Gly Leu Arg
            180                 185                 190

gct tcg gga agc aac ggg gta tta gtt gaa ggt gct tat gtt cca tta       624
Ala Ser Gly Ser Asn Gly Val Leu Val Glu Gly Ala Tyr Val Pro Leu
        195                 200                 205

cac cgg atc ttt ccg gct ggc cgg gtg atg gct cat ccg ctt ttc ttg       672
His Arg Ile Phe Pro Ala Gly Arg Val Met Ala His Pro Leu Phe Leu
    210                 215                 220

ctt ggg ttc cct tta gta tct tta ggc ggc gac gaa cga ttg gtg tca       720
Leu Gly Phe Pro Leu Val Ser Leu Gly Gly Asp Glu Arg Leu Val Ser
225                 230                 235                 240

ctt ttc caa gaa cgc act gag aag cgc att cgt gtc ttc aaa ggc ggc       768
Leu Phe Gln Glu Arg Thr Glu Lys Arg Ile Arg Val Phe Lys Gly Gly
                245                 250                 255

gcg aaa gaa aag gat tct gcc gct agc cag cgg ctg tta gcc gag atg       816
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Ala Lys Glu Lys Asp Ser Ala Ala Ser Gln Arg Leu Leu Ala Glu Met
            260                 265                 270

aaa aca gaa tta aat gca atg gaa ggc att gtg gaa caa tat atc cgc      864
Lys Thr Glu Leu Asn Ala Met Glu Gly Ile Val Glu Gln Tyr Ile Arg
        275                 280                 285

cag ctt gag gct tgc caa aaa gaa gga aag acg gtg atg aac gat atg      912
Gln Leu Glu Ala Cys Gln Lys Glu Gly Lys Thr Val Met Asn Asp Met
    290                 295                 300

gag cga gag cag cta ttc gca tgg cgt gga tat gtg gca aaa gcg tcc      960
Glu Arg Glu Gln Leu Phe Ala Trp Arg Gly Tyr Val Ala Lys Ala Ser
305                 310                 315                 320

gcc aat att gcc gtc aga aca ctg tta act ctt gga ggc aat tcg atc     1008
Ala Asn Ile Ala Val Arg Thr Leu Leu Thr Leu Gly Gly Asn Ser Ile
                325                 330                 335

ttt aaa ggc gat ccg gta gaa ctg ttc aca aga gat ttg cta gcg gtg     1056
Phe Lys Gly Asp Pro Val Glu Leu Phe Thr Arg Asp Leu Leu Ala Val
            340                 345                 350

gcc gca cat cct aac tcc ctg tgg gag gat gcg atg gct gca tat gga     1104
Ala Ala His Pro Asn Ser Leu Trp Glu Asp Ala Met Ala Ala Tyr Gly
        355                 360                 365

aga acg ata ttc ggg ctg cca ggg gac cca gtc tgg taa                 1143
Arg Thr Ile Phe Gly Leu Pro Gly Asp Pro Val Trp
    370                 375                 380
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<210> 34
<211> 380
<212> PRT
<213> Bacillus stearothermophilus

<400> 34

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Met Glu Lys Asn Lys Met Leu Ile Glu Glu Lys Leu Asp Thr Ala Ala
1               5                   10                  15

Leu Leu Ala Lys Ala Glu Glu Ile Gly Arg Ile Ala Glu Glu Glu Ala
            20                  25                  30

Gly Glu Ala Asp Arg Asn Ala Cys Phe Ser Asp Arg Val Ala Arg Ala
        35                  40                  45

Ile Lys Glu Ala Gly Phe His Lys Leu Met Arg Pro Lys Gln Tyr Gly
    50                  55                  60

Gly Leu Gln Val Asp Leu Arg Thr Tyr Gly Glu Ile Val Arg Thr Val
65                  70                  75                  80

Ala Arg Tyr Ser Val Ala Ala Gly Trp Leu Thr Tyr Phe Tyr Ser Met
                85                  90                  95

His Glu Val Trp Ala Ala Tyr Leu Pro Pro Lys Gly Arg Glu Glu Ile
            100                 105                 110

Phe Gly Gln Gly Gly Leu Leu Ala Asp Val Val Ala Pro Val Gly Arg
        115                 120                 125

Val Glu Lys Asp Gly Asp Gly Tyr Arg Leu Tyr Gly Gln Trp Asn Phe
    130                 135                 140

Cys Ser Gly Val Leu His Ser Asp Trp Ile Gly Leu Gly Ala Met Met
145                 150                 155                 160

Glu Leu Pro Asp Gly Asn Ser Pro Glu Tyr Cys Leu Leu Val Leu Pro
                165                 170                 175

Lys Ser Asp Val Gln Ile Val Glu Asn Trp Asp Thr Met Gly Leu Arg
            180                 185                 190

Ala Ser Gly Ser Asn Gly Val Leu Val Glu Gly Ala Tyr Val Pro Leu
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195 200 205

His Arg Ile Phe Pro Ala Gly Arg Val Met Ala His Pro Leu Phe Leu
210 215 220

Leu Gly Phe Pro Leu Val Ser Leu Gly Gly Asp Glu Arg Leu Val Ser
225 230 235 240

Leu Phe Gln Glu Arg Thr Glu Lys Arg Ile Arg Val Phe Lys Gly Gly
245 250 255

Ala Lys Glu Lys Asp Ser Ala Ala Ser Gln Arg Leu Leu Ala Glu Met
260 265 270

Lys Thr Glu Leu Asn Ala Met Glu Gly Ile Val Glu Gln Tyr Ile Arg
275 280 285

Gln Leu Glu Ala Cys Gln Lys Glu Gly Lys Thr Val Met Asn Asp Met
290 295 300

Glu Arg Glu Gln Leu Phe Ala Trp Arg Gly Tyr Val Ala Lys Ala Ser
305 310 315 320

Ala Asn Ile Ala Val Arg Thr Leu Leu Thr Leu Gly Gly Asn Ser Ile
325 330 335

Phe Lys Gly Asp Pro Val Glu Leu Phe Thr Arg Asp Leu Leu Ala Val
340 345 350

Ala Ala His Pro Asn Ser Leu Trp Glu Asp Ala Met Ala Ala Tyr Gly
355 360 365

Arg Thr Ile Phe Gly Leu Pro Gly Asp Pro Val Trp
370 375 380

<210> 35
<211> 1191
<212> DNA
<213> Helianthus annuus

<220>
<221> CDS
<222> (1)..(1191)

<400> 35
atg gcg att cgc atc aat acg gcg acg ttt caa tca gac ctg tac cgt 48
Met Ala Ile Arg Ile Asn Thr Ala Thr Phe Gln Ser Asp Leu Tyr Arg
1 5 10 15

tca ttc gcg ttt cct caa ccg aaa cct ctc aga tct ccc aaa ttc gcc 96
Ser Phe Ala Phe Pro Gln Pro Lys Pro Leu Arg Ser Pro Lys Phe Ala
20 25 30

atg gct tcc acc att gga tcc gct aca acg aag gtt gaa agc acc aaa 144
Met Ala Ser Thr Ile Gly Ser Ala Thr Thr Lys Val Glu Ser Thr Lys
35 40 45

aag ccc ttt acc cct cca agg gag gtt cac caa cag gtg cta cac tca 192
Lys Pro Phe Thr Pro Pro Arg Glu Val His Gln Gln Val Leu His Ser
50 55 60

atg ccg cca caa aag atc gaa atc ttc aaa tcc atg gag ggt tgg gcc 240
Met Pro Pro Gln Lys Ile Glu Ile Phe Lys Ser Met Glu Gly Trp Ala
65 70 75 80

gaa aat aac ata ttg gtt cac cta aag cct gtc gaa aaa tgc tgg caa 288
Glu Asn Asn Ile Leu Val His Leu Lys Pro Val Glu Lys Cys Trp Gln
85 90 95

gca cag gat ttc cta cca gat ccc gca tct gac gga ttt atg gaa caa 336
Ala Gln Asp Phe Leu Pro Asp Pro Ala Ser Asp Gly Phe Met Glu Gln
100 105 110

gtg gag gaa tta cgg gct cgg gct aag gag att ccg gat gat tac ttt 384

```
Val Glu Glu Leu Arg Ala Arg Ala Lys Glu Ile Pro Asp Asp Tyr Phe
        115                 120                 125

gtt gtt ttg gtt gga gat atg att act gaa gaa gca ctg cct act tac      432
Val Val Leu Val Gly Asp Met Ile Thr Glu Glu Ala Leu Pro Thr Tyr
    130                 135                 140

caa aca atg ctt aat act ctt gat ggt gtg cgt gat gag acc ggg gct      480
Gln Thr Met Leu Asn Thr Leu Asp Gly Val Arg Asp Glu Thr Gly Ala
145                 150                 155                 160

acc cta ctt ctt ggg cta gtc tgg act cgg gct tgg acc gct gaa gaa      528
Thr Leu Leu Leu Gly Leu Val Trp Thr Arg Ala Trp Thr Ala Glu Glu
                165                 170                 175

aac agg cac ggt gat ctt cta cat cag tat ctg tat ctt agt ggg cgg      576
Asn Arg His Gly Asp Leu Leu His Gln Tyr Leu Tyr Leu Ser Gly Arg
            180                 185                 190

gtc gac atg agg cag att cag aag aca att cag tac ctc att ggg tct      624
Val Asp Met Arg Gln Ile Gln Lys Thr Ile Gln Tyr Leu Ile Gly Ser
        195                 200                 205

gga atg gac ccc cgg acc gaa aac agt cct tac ctt ggg ttc atc tac      672
Gly Met Asp Pro Arg Thr Glu Asn Ser Pro Tyr Leu Gly Phe Ile Tyr
    210                 215                 220

act tca ttt caa gag cgt gcc acc ttc atc tct cac gga aac aca gcc      720
Thr Ser Phe Gln Glu Arg Ala Thr Phe Ile Ser His Gly Asn Thr Ala
225                 230                 235                 240

cgg cac gca aag gag cat ggt gac gtg aag ctg gct caa atg tgc ggt      768
Arg His Ala Lys Glu His Gly Asp Val Lys Leu Ala Gln Met Cys Gly
                245                 250                 255

ata att gca gct gat gaa aaa agg cac gaa acc gcc tac aca aaa ata      816
Ile Ile Ala Ala Asp Glu Lys Arg His Glu Thr Ala Tyr Thr Lys Ile
            260                 265                 270

gta gaa aaa ctc ttc gaa att gac ccg gac ggc act gtt ctc gct ttt      864
Val Glu Lys Leu Phe Glu Ile Asp Pro Asp Gly Thr Val Leu Ala Phe
        275                 280                 285

gcc gac atg atg agg aaa aag atc tcc atg cct gca cac ttg atg tac      912
Ala Asp Met Met Arg Lys Lys Ile Ser Met Pro Ala His Leu Met Tyr
    290                 295                 300

gat ggg cgt gat gat aac ctc ttc gaa aat ttc tca gct gtt gcc caa      960
Asp Gly Arg Asp Asp Asn Leu Phe Glu Asn Phe Ser Ala Val Ala Gln
305                 310                 315                 320

agg ctc ggt gtg tac act gcg aag gac tat gca gac att ctg gag ttt     1008
Arg Leu Gly Val Tyr Thr Ala Lys Asp Tyr Ala Asp Ile Leu Glu Phe
                325                 330                 335

ctg gtg ggc cgg tgg aag gtg gcg gat tta acc ggg ctt tct ggt gaa     1056
Leu Val Gly Arg Trp Lys Val Ala Asp Leu Thr Gly Leu Ser Gly Glu
            340                 345                 350

ggg cgt aaa gcc caa gac tat gtg tgc ggg ctg gcc cca aga atc aga     1104
Gly Arg Lys Ala Gln Asp Tyr Val Cys Gly Leu Ala Pro Arg Ile Arg
        355                 360                 365

agg ctt gag gag agg aac tcg gca agg gcg aag gaa agt gtg aac gtt     1152
Arg Leu Glu Glu Arg Asn Ser Ala Arg Ala Lys Glu Ser Val Asn Val
    370                 375                 380

ccg ttc agc tgg atc ttt gat aga gaa gtg aag ctc tga                1191
Pro Phe Ser Trp Ile Phe Asp Arg Glu Val Lys Leu
385                 390                 395
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<210> 36
<211> 396
<212> PRT
<213> Helianthus annuus

<400> 36

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Lys Pro Phe Thr Pro Pro Arg Glu Val His Gln Gln Val Leu His Ser
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Met Pro Pro Gln Lys Ile Glu Ile Phe Lys Ser Met Glu Gly Trp Ala
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Glu Asn Asn Ile Leu Val His Leu Lys Pro Val Glu Lys Cys Trp Gln
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Ala Gln Asp Phe Leu Pro Asp Pro Ala Ser Asp Gly Phe Met Glu Gln
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Val Glu Glu Leu Arg Ala Arg Ala Lys Glu Ile Pro Asp Asp Tyr Phe
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Val Val Leu Val Gly Asp Met Ile Thr Glu Glu Ala Leu Pro Thr Tyr
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Gln Thr Met Leu Asn Thr Leu Asp Gly Val Arg Asp Glu Thr Gly Ala
145 150 155 160

Thr Leu Leu Leu Gly Leu Val Trp Thr Arg Ala Trp Thr Ala Glu Glu
165 170 175

Asn Arg His Gly Asp Leu Leu His Gln Tyr Leu Tyr Leu Ser Gly Arg
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Gly Met Asp Pro Arg Thr Glu Asn Ser Pro Tyr Leu Gly Phe Ile Tyr
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Arg His Ala Lys Glu His Gly Asp Val Lys Leu Ala Gln Met Cys Gly
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Ile Ile Ala Ala Asp Glu Lys Arg His Glu Thr Ala Tyr Thr Lys Ile
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Val Glu Lys Leu Phe Glu Ile Asp Pro Asp Gly Thr Val Leu Ala Phe
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Arg Leu Gly Val Tyr Thr Ala Lys Asp Tyr Ala Asp Ile Leu Glu Phe
325 330 335

Leu Val Gly Arg Trp Lys Val Ala Asp Leu Thr Gly Leu Ser Gly Glu
340 345 350

Gly Arg Lys Ala Gln Asp Tyr Val Cys Gly Leu Ala Pro Arg Ile Arg
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Arg Leu Glu Glu Arg Asn Ser Ala Arg Ala Lys Glu Ser Val Asn Val
370 375 380

Pro Phe Ser Trp Ile Phe Asp Arg Glu Val Lys Leu
385 390 395

CLAIMS

1. A method of carrying out an oxidation reaction catalysed by a monooxygenase enzyme and using hydrogen peroxide as an oxidant, in which reaction a low level of oxidation damage of the monooxygenase occurs, said method comprising producing the hydrogen peroxide simultaneously with the oxidation reaction, wherein the hydrogen peroxide is produced at a rate less than or equal to the rate at which it is used in the reaction.

2. A method according to claim 1, wherein the monooxygenase enzyme has a K_m for H_2O_2 of at least 15nM.

3. A method according to claim 1 or 2, wherein the monooxygenase enzyme is a P450 enzyme.

4. A method according to any one of the preceding claims, wherein the rate of H_2O_2 production is less than or equal to 3 μg per mg of enzyme.

5. A method according to any one of the preceding claims, wherein the concentration of H_2O_2 throughout the reaction is less than or equal to 1 mM.

6. A method according to any one of the preceding claims, wherein the reaction continues for at least 240 minutes.

7. A method according to any one of the preceding claims, wherein the H_2O_2 is produced by an electrochemical reaction.

8. A method according to any one of claims 1 to 6, wherein the H_2O_2 is produced by an enzyme reaction.

9. A method according to claim 8, wherein the enzyme is glucose oxidase.

10. A method according to any one of claims 1 to 6, wherein the H_2O_2 is produced by a H_2O_2 precursor.

11. A method according to claim 10, wherein the H_2O_2 precursor is perborate, percarbonate or perphosphate.

12. A method according to any one of the preceding claims, wherein the substrate which is oxidised by the monooxygenase enzyme is an alkane, aromatic compound, terpenoid compound, alkene or fatty acid.

13. Use of electrodes for producing H_2O_2 to drive an oxidation reaction as defined in claim 7.

14. Use of an enzyme for producing H_2O_2 to drive an oxidation reaction as defined in claim 8 or 9.

15. Use of perborate, percarbonate or perphosphate for producing H_2O_2 to drive an oxidation reaction as defined in claim 10.

16. A method of carrying out an oxidation reaction catalysed by a monooxygenase enzyme and using hydrogen peroxide as an oxidant, in which reaction a low level of oxidation damage of the monooxygenase occurs, said method comprising carrying out the reaction in the presence of an H_2O_2 or hydroxyl radical sequestering agent that controls the H_2O_2 or hydroxyl radical concentration.

17. A method according to claim 16, wherein the sequestering agent is EDTA.